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(71) Applicants (for all designated States except US): SAGAMI  
 CHEMICAL RESEARCH CENTER (JP/PI): 4-1,  
 Nishi-Ohnuma 4-chome, Sagami-shi, Kanagawa  
 229-0012 (JP), PROTEGENE INC. (JP/PI): 2-20-3,  
 Naka-cho, Meguro-ku, Tokyo 153-0065 (JP).

(72) Inventors and  
 Applicants (for US only): KATO, Seichi (JP/PI):  
 3-46-50, Wakamatsu, Sagami-shi, Kanagawa  
 229-0014 (JP), KIMURA, Tomoko (JP/PI): 302, 4-1-28,  
 Nishikura, Tama-shi, Kawasaki-shi, Kanagawa 214-0037  
 (JP).

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(74) Agents: AOYAMA, Taro et al.; Aoyama & Partners,  
 IMP Building, 3-7, Shiroani 1-chome, Chuo-ku, Osaka-shi,  
 Osaka 540-0001 (JP).

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(54) Title: HUMAN PROTEINS HAVING HYDROPHOBIC DOMAINS AND DNAs ENCODING THESE PROTEINS

(57) Abstract

The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs.

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## DESCRIPTION

Human Proteins Having Hydrophobic  
Domains and DNAs Encoding These Proteins

## TECHNICAL FIELD

The present invention relates to human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. The proteins of the present invention can be employed as pharmaceuticals or as antigens for preparing antibodies against these proteins. The human cDNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the cDNAs can be utilized as gene sources for large-scale production of the proteins encoded by these cDNAs. Cells into which these genes are introduced to express secretory proteins and membrane proteins in large amounts can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

## BACKGROUND ART

Cells secrete many proteins outside the cells. These secretory proteins play important roles for the proliferation control, the differentiation induction, the material transportation, the biological protection, etc. in the cells. Different from intracellular proteins, the secretory proteins exert their actions outside the cells, whereby they can be administered in the intracorporeal manner such as the injection or the drip, so that there are

hidden potentialities as medicines. In fact, a number of human secretory proteins such as interferons, interleukins, erythropoietin, thrombolytic agents, etc. have been currently employed as medicines. In addition, secretory proteins other than those described above have been undergoing clinical trials to develop as pharmaceuticals. Because it has been conceived that the human cells still produce many unknown secretory proteins, availability of these secretory proteins as well as genes coding for them is expected to lead to development of novel pharmaceuticals utilizing these proteins.

On the other hand, membrane proteins play important roles, as signal receptors, ion channels, transporters, etc. in the material transportation and the information transmission through the cell membrane. Examples thereof include receptors for a variety of cytokines, ion channels for the sodium ion, the potassium ion, the chloride ion, etc., transporters for saccharides and amino acids, and so on, where the genes for many of them have been cloned already. It has been clarified that abnormalities of these membrane proteins are associated with a number of hitherto cryptogenic diseases. Therefore, discovery of a new membrane protein is anticipated to lead to elucidation of the causes of many diseases, so that isolation of a new gene coding for the membrane protein has been desired.

Heretofore, owing to difficulty in the purification from human cells, these secretory proteins and membrane proteins have been isolated by an approach from the gene side. A general method is the so-called expression cloning which comprises introduction of a cDNA library into eucaryotic cells to express cDNAs and then screening of the cells secreting, or expressing on the surface of membrane,

the objective active protein. However, this method is applicable only to cloning of a gene for a protein with a known function.

In general, secretory proteins and membrane proteins possess at least one hydrophobic domain inside the proteins, wherein, after synthesis thereof in the ribosome, this domain works as a secretory signal or remains in the phospholipid membrane to be trapped in the membrane. Accordingly, the evidence of this cDNA for encoding a secretory protein and a membrane protein is provided by determination of the whole base sequence of a full-length cDNA followed by detection of highly hydrophobic domain(s) in the amino acid sequence of the protein encoded by this cDNA.

#### OBJECTS OF THE INVENTION

The main object of the present invention is to provide novel human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as transformed eucaryotic cells that are capable of expressing these DNAs. This object as well as other objects and advantages of the present invention will become apparent to those skilled in the art from the following description with reference to the accompanying drawings.

#### BRIEF DESCRIPTION OF DRAWINGS

Fig. 1 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01550.

Fig. 2 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02593.

Fig. 3 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10195.

Fig. 4 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10423.

Fig. 5 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10506.

Fig. 6 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10507.

Fig. 7 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10548.

Fig. 8 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10566.

Fig. 9 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10567.

Fig. 10 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10568.

Fig. 11 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01426.

Fig. 12 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02515.

Fig. 13 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02575.

Fig. 14 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10357.

Fig. 15 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10447.

Fig. 16 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10477.

Fig. 17 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10513.

Fig. 18 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10540.

Fig. 19 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10557.

Fig. 20 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10563.

Fig. 21 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01467.

Fig. 22 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01956.

Fig. 23 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02545.

Fig. 24 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02551.

Fig. 25 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 26 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02632.

Fig. 27 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10488.

Fig. 28 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10538.

Fig. 29 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10542.

Fig. 30 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10571.

Fig. 31 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01470.

Fig. 32 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02419.

Fig. 33 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02631.

Fig. 34 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02695.

Fig. 35 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10031.

Fig. 36 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10530.

Fig. 37 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10541.

Fig. 38 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10550.

Fig. 39 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10590.

Fig. 40 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10591.

Fig. 41 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP01462.

Fig. 42 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02485.

Fig. 43 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP02798.

Fig. 44 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10041.

Fig. 45 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10246.

Fig. 46 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10392.

Fig. 47 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10489.

Fig. 48 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10519.

Fig. 49 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10531.

Fig. 50 illustrates the hydrophobicity/hydrophilicity profile of the protein encoded by clone HP10574.

#### SUMMARY OF THE INVENTION



As the result of intensive studies, the present inventors have been successful in cloning of cDNAs coding for proteins having hydrophobic domains from the human full-length cDNA bank, thereby completing the present invention. In other words, the present invention provides human proteins having hydrophobic domains, namely proteins comprising any of the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. Moreover, the present invention provides DNAs coding for the above-mentioned proteins, exemplified by cDNAs comprising any of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140, as well as expression vectors that are capable of expressing any of these DNAs by in vitro translation or in eucaryotic cells and transformed eucaryotic cells that are capable of expressing these DNAs and of producing the above-mentioned proteins.

#### DETAILED DESCRIPTION OF THE INVENTION

The proteins of the present invention can be obtained, for example, by a method for isolation from human organs, cell lines, etc., a method for preparation of peptides by the chemical synthesis, or a method for production with the recombinant DNA technology using the DNAs coding for the hydrophobic domains of the present invention, among which the method for production with the recombinant DNA technology is employed preferably. For instance, in vitro expression of the proteins can be achieved by preparation of an RNA by in vitro transcription from a vector having one of the cDNAs of the present invention, followed by in vitro translation using this RNA as a template. Also, introduction of the translated region into a suitable expression vector

by the method known in the art leads to expression of a large amount of the encoded protein in prokaryotic cells such as *Escherichia coli*, *Bacillus subtilis*, etc., and eucaryotic cells such as yeasts, insect cells, mammalian cells, etc.

In the case where one of the proteins of the present invention is produced by expressing the DNA by in vitro translation, the protein of the present invention can be produced in vitro, when the translated region of this cDNA is introduced into a vector having an RNA polymerase promoter, followed by addition of the vector to an in vitro translation system such as a rabbit reticulocyte lysate or a wheat germ extract, containing an RNA polymerase corresponding to the promoter. RNA polymerase promoters are exemplified by T<sub>7</sub>, T<sub>3</sub>, SP6, and the like. The vectors containing these RNA polymerase promoters are exemplified by pKA1, pCDM8, pT3/T7 18, pT7/3 19, pBluescript II, and so on. Furthermore, the protein of the present invention can be expressed as the secreted form or the form incorporated into the microsome membrane, when a canine pancreas microsome or the like is added to the reaction system.

In the case where one of the protein of the present invention is produced by expressing the DNA in a microorganism such as *Escherichia coli* etc., a recombinant expression vector bearing the translated region of the cDNA of the present invention is constructed in an expression vector having an origin which can be replicated in the microorganism, a promoter, a ribosome-binding site, a cDNA-cloning site, a terminator etc. and, after transformation of the host cells with this expression vector, the resulting transformant is incubated, whereby the protein encoded by said cDNA can be produced on a large scale in the

microorganism. In this case, a protein fragment containing any region can be obtained by carrying out the expression with inserting an initiation codon and a termination codon in front of and behind the selected translated region.

Alternatively, a fusion protein with another protein can be expressed. Only the portion of the protein encoded by this cDNA can be obtained by cleavage of this fusion protein with a suitable protease. The expression vector for *Escherichia coli* is exemplified by the pUC series, pBluescript II, the pET expression system, the pGEX expression system, and so on.

In the case where one of the proteins of the present invention is produced by expressing the DNA in eucaryotic cells, the protein of the present invention can be produced as a secretory protein or as a membrane protein on the cell-membrane surface, when the translated region of this cDNA is introduced into an expression vector for eucaryotic cells that has a promoter, a splicing region, a poly(A) addition site, etc., followed by introduction into the eucaryotic cells. The expression vector is exemplified by pXal, pED6dpc2, pCDM8, pSVK3, pMSG, pSVL, pBK-CMV, pBK-RSV, EBV vector, pRS, pYES2, and so on. Examples of eucaryotic cells to be used in general include mammalian cultured cells such as simian kidney cells COS7, Chinese hamster ovary cells CHO, etc., budding yeasts, fission yeasts, silkworm cells, *Xenopus* oocytes, and so on, but any eucaryotic cells may be used, provided that they are capable of expressing the proteins of the present invention. The expression vector can be introduced into the eucaryotic cells by methods known in the art such as the electroporation method, the calcium phosphate method, the liposome method, the DEAE-dextran method, and so on.

After one of the proteins of the present invention is

expressed in prokaryotic cells or eucaryotic cells, the objective protein can be isolated from the culture and purified by a combination of separation procedures known in the art. Such examples include treatment with a denaturing agent such as urea or a detergent, sonication, enzymatic digestion, salting-out or solvent precipitation, dialysis, centrifugation, ultrafiltration, gel filtration, SDS-PAGE, isoelectric focusing, ion-exchange chromatography, hydrophobic chromatography, affinity chromatography, reverse phase chromatography, and so on.

The proteins of the present invention include peptide fragments (5 amino acid residues or more) containing any partial amino acid sequence in the amino acid sequences represented by SEQ ID Nos. 1. to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130. These peptide fragments can be utilized as antigens for preparation of antibodies. Hereupon, among the proteins of the present invention, those having the signal sequences are secreted in the form of mature proteins, after the signal sequences are removed. Therefore, these mature proteins shall come within the scope of the present invention. The N-terminal amino acid sequences of the mature proteins can be easily determined by using the method for the determination of cleavage site of a signal sequence [JP 8-187100 A]. Furthermore, some membrane proteins undergo the processing on the cell surface to be converted to the secretory forms. Such proteins or peptides in the secretory forms shall come within the scope of the present invention. In the case where sugar chain-binding sites are present in the amino acid sequences, expression in appropriate eucaryotic cells affords proteins to which sugar chains are attached. Accordingly, such proteins or peptides to which sugar chains are attached shall come within the

scope of the present invention.

The DNAs of the present invention include all the DNAs coding for the above-mentioned proteins. These DNAs can be obtained by using a method by chemical synthesis, a method by cDNA cloning, and so on.

The cDNAs of the present invention can be cloned, for example, from cDNA libraries derived from the human cells. These cDNAs are synthesized by using as templates poly(A)<sup>+</sup> RNAs extracted from human cells. The human cells may be cells delivered from the human body, for example, by the operation or may be the cultured cells. The cDNAs can be synthesized by using any method selected from the Okayama-Berg method [Okayama, H. and Berg, P., Mol. Cell. Biol. 2: 161-170 (1982)], the Gubler-Hoffman method [Gubler, U. and Hoffman, J. Gene 25: 263-269 (1983)], and so on, but it is preferred to use the capping method [Kato, S. et al., Gene 150: 243-250 (1994)], as exemplified in Examples, in order to obtain a full-length clone in an effective manner. In addition, commercially available, human cDNA libraries can be utilized. Cloning of the cDNAs of the present invention from the cDNA libraries can be carried out by synthesis of an oligonucleotide on the basis of base sequences of any portion in the cDNA of the present invention, followed by screening using this oligonucleotide as the probe according to the colony or plaque hybridization by a method known in the art. In addition, the cDNA fragments of the present invention can be prepared by synthesis of oligonucleotides which hybridize with both termini of the objective cDNA fragment, followed by the usage of these oligonucleotides as the primers for the RT-PCR method using an mRNA isolated from human cells.

The cDNAs of the present invention are characterized by

comprising either of the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Table 1 summarizes the clone number (HP number), the cells from which the cDNA was obtained, the total base number of the cDNA, and the number of the amino acid residues of the encoded protein, for each of the cDNAs.

Table 1

SEQ ID No.	HP number	Cells	Base number	Number of amino acid residues
1, 11, 21	HP01550	Stomach cancer	510	125
2, 12, 22	HP02593	Saos-2	697	131
3, 13, 23	HP10195	HT-1080	1619	242
4, 14, 24	HP10423	U-2 OS	1066	264
5, 15, 25	HP10506	Stomach cancer	618	112
6, 16, 26	HP10507	Stomach cancer	1021	146
7, 17, 27	HP10548	Stomach cancer	1432	344
8, 18, 28	HP10566	Stomach cancer	601	97
9, 19, 29	HP10567	Stomach cancer	585	124
10, 20, 30	HP10568	Stomach cancer	1100	327
31, 41, 51	HP01426	Stomach cancer	1065	313
32, 42, 52	HP02515	Saos-2	937	229
33, 43, 53	HP02575	Saos-2	1678	467
34, 44, 54	HP10357	Stomach cancer	467	99
35, 45, 55	HP10447	Liver	875	189
36, 46, 56	HP10477	Liver	1256	363
37, 47, 57	HP10513	Stomach cancer	884	249
38, 48, 58	HP10540	Saos-2	589	98
39, 49, 59	HP10557	Stomach cancer	673	172
40, 50, 60	HP10563	Saos-2	1425	120
61, 71, 81	HP01467	HT-1080	1436	307
62, 72, 82	HP01956	Liver	997	183
63, 73, 83	HP02545	Saos-2	1753	327
64, 74, 84	HP02551	Saos-2	1117	223
65, 75, 85	HP02631	Saos-2	1380	48
66, 76, 86	HP02632	HT-1080	1503	371
67, 77, 87	HP10488	Liver	733	90
68, 78, 88	HP10538	Saos-2	3768	499
69, 79, 89	HP10542	Stomach cancer	770	106
70, 80, 90	HP10571	Stomach cancer	1229	152

91, 101, 111	HP01470	Stomach cancer	1619	358
92, 102, 112	HP02419	Stomach cancer	2054	226
93, 103, 113	HP02631	Saos-2	1380	195
94, 104, 114	HP02695	Stomach cancer	1292	339
95, 105, 115	HP10031	Saos-2	2168	487
96, 106, 116	HP10530	Saos-2	1357	393
97, 107, 117	HP10541	Stomach cancer	711	196
98, 108, 118	HP10550	Stomach cancer	651	107
99, 109, 119	HP10590	HT-1080	1310	350
100, 110, 120	HP10591	HT-1080	1400	107
121, 131, 141	HP01462	HT-1080	2050	483
122, 132, 142	HP02485	Stomach cancer	2746	334
123, 133, 143	HP02798	HT-1080	1136	267
124, 134, 144	HP10041	Saos-2	619	106
125, 135, 145	HP10246	KB	864	224
126, 136, 146	HP10392	U-2 OS	1527	258
127, 137, 147	HP10489	Stomach cancer	659	110
128, 138, 148	HP10519	Stomach cancer	710	91
129, 139, 149	HP10531	Saos-2	2182	344
130, 140, 150	HP10574	Stomach cancer	2773	428

Hereupon, the same clones as the cDNAs of the present invention can be easily obtained by screening of the cDNA libraries constructed from the human cell lines or human tissues utilized in the present invention by the use of an oligonucleotide probe synthesized on the basis of the cDNA base sequence described in any of SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and 131 to 150.

In general, the polymorphism due to the individual difference is frequently observed in human genes. Accordingly, any cDNA in which one or plural nucleotides are inserted, deleted and/or substituted with other nucleotides in SEQ ID Nos. 11 to 30, 41 to 60, 71 to 90, 101 to 120, and

131 to 150 shall come within the scope of the present invention.

In a similar manner, any protein in which one or plural amino acids are inserted, deleted and/or substituted with other amino acids shall come within the scope of the present invention, as far as the protein possesses the activity of any protein having the amino acid sequences represented by SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.

The cDNAs of the present invention include cDNA fragments (10 bp or more) containing any partial base sequence in the base sequences represented by SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140 or in the base sequences represented by SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150. Also, DNA fragments consisting of a sense strand and an anti-sense strand shall come within this scope. These DNA fragments can be utilized as the probes for the genetic diagnosis.

In addition to the activities and uses described above, the polynucleotides and proteins of the present invention may exhibit one or more of the uses or biological activities (including those associated with assays cited herein) identified below. Uses or activities described for proteins of the present invention may be provided by administration or use of such proteins or by administration or use of polynucleotides encoding such proteins (such as, for example, in gene therapies or vectors suitable for introduction of DNA).

#### Research Uses and Utilities

The polynucleotides provided by the present invention can be used by the research community for various purposes. The polynucleotides can be used to express recombinant

protein for analysis, characterization or therapeutic use; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in disease states); as molecular weight markers on Southern gels; as chromosome markers or tags (when labeled) to identify chromosomes or to map related gene positions; to compare with endogenous DNA sequences in patients to identify potential genetic disorders; as probes to hybridize and thus discover novel, related DNA sequences; as a source of information to derive PCR primers for genetic fingerprinting; as a probe to "subtract-out" known sequences in the process of discovering other novel polynucleotides; for selecting and making oligomers for attachment to a "gene chip" or other support, including for examination of expression patterns; to raise anti-protein antibodies using DNA immunization techniques; and as an antigen to raise anti-DNA antibodies or elicit another immune response. Where the polynucleotide encodes a protein which binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the polynucleotide can also be used in interaction trap assays (such as, for example, that described in Gyuris et al., Cell 75:791-803 (1993)) to identify polynucleotides encoding the other protein with which binding occurs or to identify inhibitors of the binding interaction.

The proteins provided by the present invention can similarly be used in assay to determine biological activity, including in a panel of multiple proteins for high-throughput screening; to raise antibodies or to elicit another immune response; as a reagent (including the labeled reagent) in assays designed to quantitatively determine

5 levels of the protein (or its receptor) in biological fluids; as markers for tissues in which the corresponding protein is preferentially expressed (either constitutively or at a particular stage of tissue differentiation or development or in a disease state); and, of course, to isolate correlative receptors or ligands. Where the protein binds or potentially binds to another protein (such as, for example, in a receptor-ligand interaction), the protein can be used to identify the other protein with which binding occurs or to identify inhibitors of the binding interaction. proteins involved in these binding interactions can also be used to screen for peptide or small molecule inhibitors or agonists of the binding interaction.

Any or all of these research utilities are capable of being developed into reagent grade or kit format for commercialization as research products.

Methods for performing the uses listed above are well known to those skilled in the art. References disclosing such methods include without limitation "Molecular Cloning: A Laboratory Manual", 2d ed., Cold Spring Harbor Laboratory Press, Sambrook, J., E.F. Fritsch and T. Maniatis eds., 1989, and "Methods in Enzymology: Guide to Molecular Cloning Techniques", Academic Press, Berger, S.L. and A.R. Kimmel eds., 1987.

#### 25 Nutritional Uses

Polynucleotides and proteins of the present invention can also be used as nutritional sources or supplements. Such uses include without limitation use as a protein or amino acid supplement, use as a carbon source, use as a nitrogen source and use as a source of carbohydrate. In such cases the protein or polynucleotide of the invention can be added to the feed of a particular organism or can be

administered as a separate solid or liquid preparation, such as in the form of powder, pills, solutions, suspensions or capsules. In the case of microorganisms, the protein or polynucleotide of the invention can be added to the medium in or on which the microorganism is cultured.

#### 5 Cytokine and Cell Proliferation/Differentiation Activity

A protein of the present invention may exhibit cytokine, cell proliferation (either inducing or inhibiting) or cell differentiation (either inducing or inhibiting) activity or may induce production of other cytokines in certain cell populations. Many protein factors discovered to date, including all known cytokines, have exhibited activity in one or more factor dependent cell proliferation assays, and hence the assays serve as a convenient confirmation of cytokine activity. The activity of a protein of the present invention is evidenced by any one of a number of routine factor dependent cell proliferation assays for cell lines including, without limitation, 32D, DA2, DA1G, T10, B9, B9/11, BaF3, MC9/G, M+ (preB M+), 2E8, RB5, DA1, 123, T1i65, HT2, CTLL2, TF-1, Mo7e and CMK.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assays for T-cell or thymocyte proliferation include without limitation those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Bertagnolli et al., J. Immunol. 145:1706-1712, 1990; Bertagnolli et al., Cellular

Immunology 133:327-341, 1991; Bertagnoli, et al., J. Immunol. 149:3778-3783, 1992; Bowman et al., J. Immunol. 152: 1756-1761, 1994.

Assays for cytokine production and/or proliferation of spleen cells, lymph node cells or thymocytes include, without limitation, those described in: Polyclonal T cell stimulation, Krusbeek, A.M. and Shevach, E.M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.12.1-3.12.14, John Wiley and Sons, Toronto. 1994; and Measurement of mouse and human Interferon  $\gamma$ , Schreiber, R.D. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.8.1-6.8.8, John Wiley and Sons, Toronto. 1994.

Assays for proliferation and differentiation of hematopoietic and lymphopoietic cells include, without limitation, those described in: Measurement of Human and Murine Interleukin 2 and Interleukin 4, Bottomly, K., Davis, L.S. and Lipsky, P.E. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.3.1-6.3.12, John Wiley and Sons, Toronto. 1991; devries et al., J. Exp. Med. 173:1205-1211, 1991; Moreau et al., Nature 336:690-692, 1988; Greenberger et al., Proc. Natl. Acad. Sci. U.S.A. 80:2931-2938, 1983; Measurement of mouse and human interleukin 6- Nordan, R. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.6.1-6.6.5, John Wiley and Sons, Toronto. 1991; Smith et al., Proc. Natl. Acad. Sci. U.S.A. 83:1857-1861, 1986; Measurement of human Interleukin 11 - Bennett, F., Giannotti, J., Clark, S.C. and Turner, K. J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 6.15.1 John Wiley and Sons, Toronto. 1991; Measurement of mouse and human Interleukin 9 - Ciarletta, A., Giannotti, J., Clark, S.C. and Turner, K.J. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp.

6.13.1, John Wiley and Sons, Toronto. 1991.

Assays for T-cell clone responses to antigens (which will identify, among others, proteins that affect APC-T cell interactions as well as direct T-cell effects by measuring proliferation and cytokine production) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Krusbeek, D.H. Margules, E.M. Shevach, W strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function; Chapter 6, Cytokines and their cellular receptors; Chapter 7, Immunologic studies in Humans); Weinberger et al., Proc. Natl. Acad. Sci. USA 77:6091-6095, 1980; Weinberger et al., Eur. J. Immun. 11:405-411, 1981; Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988.

#### Immune Stimulating or Suppressing Activity

A protein of the present invention may also exhibit immune stimulating or immune suppressing activity, including without limitation the activities for which assays are described herein. A protein may be useful in the treatment of various immune deficiencies and disorders (including severe combined immunodeficiency (SCID)), e.g., in regulating (up or down) growth and proliferation of T and/or B lymphocytes, as well as affecting the cytolytic activity of NK cells and other cell populations. These immune deficiencies may be genetic or be caused by viral (e.g., HIV) as well as bacterial or fungal infections, or may result from autoimmune disorders. More specifically, infectious diseases caused by viral, bacterial, fungal or other infection may be treatable using a protein of the present invention, including infections by HIV, hepatitis viruses, herpesviruses, mycobacteria, leishmania spp., malaria spp.

and various fungal infections such as candidiasis. Of course, in this regard, a protein of the present invention may also be useful where a boost to the immune system generally may be desirable, i.e., in the treatment of cancer.

Autoimmune disorders which may be treated using a protein of the present invention include, for example, connective tissue disease, multiple sclerosis, systemic lupus erythematosus, rheumatoid arthritis, autoimmune pulmonary inflammation, Guillain-Barre syndrome, autoimmune thyroiditis, insulin dependent diabetes mellitus, myasthenia gravis, graft-versus-host disease and autoimmune inflammatory eye disease. Such a protein of the present invention may also be useful in the treatment of allergic reactions and conditions, such as asthma (particularly allergic asthma) or other respiratory problems. Other conditions, in which immune suppression is desired (including, for example, organ transplantation), may also be treatable using a protein of the present invention.

Using the proteins of the invention it may also be possible to induce immune responses, in a number of ways. Down regulation may be in the form of inhibiting or blocking an immune response already in progress or may involve preventing the induction of an immune response. The functions of activated T cells may be inhibited by suppressing T cell responses or by inducing specific tolerance in T cells, or both. Immunosuppression of T cell responses is generally an active, non-antigen-specific, process which requires continuous exposure of the T cells to the suppressive agent. Tolerance, which involves inducing non-responsiveness or anergy in T cells, is distinguishable from immunosuppression in that it is generally antigen-specific and persists after exposure to the tolerizing agent

has ceased. Operationally, tolerance can be demonstrated by the lack of a T cell response upon reexposure to specific antigen in the absence of the tolerizing agent.

Down regulating or preventing one or more antigen functions (including without limitation B lymphocyte antigen functions (such as , for example, B7)), e.g., preventing high level lymphokine synthesis by activated T cells, will be useful in situations of tissue, skin and organ transplantation and in graft-versus-host disease (GVHD). For example, blockage of T cell function should result in reduced tissue destruction in tissue transplantation. Typically, in tissue transplants, rejection of the transplant is initiated through its recognition as foreign by T cells, followed by an immune reaction that destroys the transplant. The administration of a molecule which inhibits or blocks interaction of a B7 lymphocyte antigen with its natural ligand(s) on immune cells (such as a soluble, monomeric form of a peptide having B7-2 activity alone or in conjunction with a monomeric form of a peptide having an activity of another B lymphocyte antigen (e.g., B7-1, B7-3) or blocking antibody), prior to transplantation can lead to the binding of the molecule to the natural ligand(s) on the immune cells without transmitting the corresponding costimulatory signal. Blocking B lymphocyte antigen function in this matter prevents cytokine synthesis by immune cells, such as T cells, and thus acts as an immunosuppressant. Moreover, the lack of costimulation may also be sufficient to anergize the T cells, thereby inducing tolerance in a subject. Induction of long-term tolerance by B lymphocyte antigen-blocking reagents may avoid the necessity of repeated administration of these blocking reagents. To achieve sufficient immunosuppression or



tolerance in a subject, it may also be necessary to block the function of a combination of B lymphocyte antigens.

The efficacy of particular blocking reagents in preventing organ transplant rejection or GVHD can be assessed using animal models that are predictive of efficacy in humans. Examples of appropriate systems which can be used include allogeneic cardiac grafts in rats and xenogeneic pancreatic islet cell grafts in mice, both of which have been used to examine the immunosuppressive effects of CTLA4Ig fusion proteins in vivo as described in Lenschow et al., Science 257:789-792 (1992) and Turka et al., Proc. Natl. Acad. Sci USA, 89:11102-11105 (1992). In addition, murine models of GVHD (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 846-847) can be used to determine the effect of blocking B lymphocyte antigen function in vivo on the development of that disease.

Blocking antigen function may also be therapeutically useful for treating autoimmune diseases. Many autoimmune disorders are the result of inappropriate activation of T cells that are reactive against self tissue and which promote the production of cytokines and autoantibodies involved in the pathology of the diseases. Preventing the activation of autoreactive T cells may reduce or eliminate disease symptoms. Administration of reagents which block costimulation of T cells by disrupting receptor:ligand interactions of B lymphocyte antigens can be used to inhibit T cell activation and prevent production of autoantibodies or T cell-derived cytokines which may be involved in the disease process. Additionally, blocking reagents may induce antigen-specific tolerance of autoreactive T cells which could lead to long-term relief from the disease. The efficacy of blocking reagents in preventing or alleviating

autoimmune disorders can be determined using a number of well-characterized animal models of human autoimmune diseases. Examples include murine experimental autoimmune encephalitis, systemic lupus erythematosus in MRL/lpr/lpr mice or NZB hybrid mice, murine autoimmune collagen arthritis, diabetes mellitus in NOD mice and BB rats, and murine experimental myasthenia gravis (see Paul ed., Fundamental Immunology, Raven Press, New York, 1989, pp. 840-856).

Upregulation of an antigen function (preferably a B lymphocyte antigen function), as a means of up regulating immune responses, may also be useful in therapy. Upregulation of immune responses may be in the form of enhancing an existing immune response or eliciting an initial immune response. For example, enhancing an immune response through stimulating B lymphocyte antigen function may be useful in cases of viral infection. In addition, systemic viral diseases such as influenza, the common cold, and encephalitis might be alleviated by the administration of stimulatory forms of B lymphocyte antigens systemically.

Alternatively, anti-viral immune responses may be enhanced in an infected patient by removing T cells from the patient, costimulating the T cells in vitro with viral antigen-pulsed APCs either expressing a peptide of the present invention or together with a stimulatory form of a soluble peptide of the present invention and reintroducing the in vitro activated T cells into the patient. Another method of enhancing anti-viral immune responses would be to isolate infected cells from a patient, transfect them with a nucleic acid encoding a protein of the present invention as described herein such that the cells express all or a portion of the protein on their surface, and reintroduce the

transfected cells into the patient. The infected cells would now be capable of delivering a costimulatory signal to, and thereby activate, T cells in vivo.

In another application, up regulation or enhancement of antigen function (preferably B lymphocyte antigen function) may be useful in the induction of tumor immunity. Tumor cells (e.g., sarcoma, melanoma, lymphoma, leukemia, neuroblastoma, carcinoma) transfected with a nucleic acid encoding at least one peptide of the present invention can be administered to a subject to overcome tumor-specific tolerance in the subject. If desired, the tumor cell can be transfected to express a combination of peptides. For example, tumor cells obtained from a patient can be transfected ex vivo with an expression vector directing the expression of a peptide having B7-2-like activity alone, or in conjunction with a peptide having B7-1-like activity and/or B7-3-like activity. The transfected tumor cells are returned to the patient to result in expression of the peptides on the surface of the transfected cell. Alternatively, gene therapy techniques can be used to target a tumor cell for transfection in vivo.

The presence of the peptide of the present invention having the activity of a B lymphocyte antigen(s) on the surface of the tumor cell provides the necessary costimulation signal to T cells to induce a T cell mediated immune response against the transfected tumor cells. In addition, tumor cells which lack MHC class I or MHC class II molecules, or which fail to reexpress sufficient amounts of MHC class I or MHC class II molecules, can be transfected with nucleic acid encoding all or a portion of (e.g., a cytoplasmic-domain truncated portion) of an MHC class I  $\alpha$  chain protein and , microglobulin protein or an MHC class

II chain protein and an MHC class II chain protein to thereby express MHC class I or MHC class II proteins on the cell surface. Expression of the appropriate class I or class II MHC in conjunction with a peptide having the activity of a B lymphocyte antigen (e.g., B7-1, B7-2, B7-3) induces a T cell mediated immune response against the transfected tumor cell. Optionally, a gene encoding an antisense construct which blocks expression of an MHC class II associated protein, such as the invariant chain, can also be cotransfected with a DNA encoding a peptide having the activity of a B lymphocyte antigen to promote presentation of tumor associated antigens and induce tumor specific immunity. Thus, the induction of a T cell mediated immune response in a human subject may be sufficient to overcome tumor-specific tolerance in the subject.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for thymocyte or splenocyte cytotoxicity include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7, Immunologic studies in Humans); Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 140:508-512, 1988; Herrmann et al., Proc. Natl. Acad. Sci. USA 78:2488-2492, 1981; Herrmann, et al., J. Immunol. 128:1968-1974, 1982; Handa et al., J. Immunol. 135:1564-1572, 1985; Takai et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J. Immunol. 137:3494-3500, 1986; Bowman et al., J.

Virology 61:1992-1998; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnoli et al., Cellular Immunology 133:327-341, 1991; Brown et al., J. Immunol. 153:3079-3092, 1994.

Assays for T-cell-dependent immunoglobulin responses and isotype switching (which will identify, among others, proteins that modulate T-cell dependent antibody responses and that affect Th1/Th2 profiles) include, without limitation, those described in: Maliszewski, J. Immunol. 144:3028-3033, 1990; and Assays for B cell function: In vitro antibody production, Mond, J.J. and Brunswick, M. In Current Protocols in Immunology. J.E.e.a. Coligan eds. Vol 1 pp. 3.8.1-3.8.16, John Wiley and Sons, Toronto. 1994.

Mixed lymphocyte reaction (MLR) assays (which will identify, among others, proteins that generate predominantly Th1 and CTL responses) include, without limitation, those described in: Current Protocols in Immunology, Ed by J. E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 3, In Vitro assays for Mouse Lymphocyte Function 3.1-3.19; Chapter 7, Immunologic studies in Humans); Takai et al., J. Immunol. 137:3494-3500, 1986; Takai et al., J. Immunol. 140:508-512, 1988; Bertagnoli et al., J. Immunol. 149:3778-3783, 1992.

Dendritic cell-dependent assays (which will identify, among others, proteins expressed by dendritic cells that activate naive T-cells) include, without limitation, those described in: Guery et al., J. Immunol. 134:536-544, 1995; Inaba et al., Journal of Experimental Medicine 173:549-559, 1991; Macatonia et al., Journal of Immunology 154:5071-5079, 1995; Porcador et al., Journal of Experimental Medicine 182:255-260, 1995; Nair et al., Journal of Virology 67:4062-4069, 1993; Huang et al., Science 264:961-965,

1994; Macatonia et al., Journal of Experimental Medicine 169:1255-1264, 1989; Bhardwaj et al., Journal of Clinical Investigation 94:797-807, 1994; and Inaba et al., Journal of Experimental Medicine 172:631-640, 1990.

Assays for lymphocyte survival/apoptosis (which will identify, among others, proteins that prevent apoptosis after superantigen induction and proteins that regulate lymphocyte homeostasis) include, without limitation, those described in: Darzynkiewicz et al., Cytometry 13:795-808, 1992; Gorczyca et al., Leukemia 7:659-670, 1993; Gorczyca et al., Cancer Research 53:1945-1951, 1993; Itoh et al., Cell 66:233-243, 1991; Zacharchuk, Journal of Immunology 145:4037-4045, 1990; Zamal et al., Cytometry 14:891-897, 1993; Gorczyca et al., International Journal of Oncology 1:639-648, 1992.

Assays for proteins that influence early steps of T-cell commitment and development include, without limitation, those described in: Antica et al., Blood 84:111-117, 1994; Fine et al., Cellular Immunology 155:111-122, 1994; Galy et al., Blood 85:2770-2778, 1995; Toki et al., Proc. Nat. Acad. Sci. USA 88:7548-7551, 1991.

#### Hematopoiesis Regulating Activity

A protein of the present invention may be useful in regulation of hematopoiesis and, consequently, in the treatment of myeloid or lymphoid cell deficiencies. Even marginal biological activity in support of colony forming cells or of factor-dependent cell lines indicates involvement in regulating hematopoiesis, e.g. in supporting the growth and proliferation of erythroid progenitor cells alone or in combination with other cytokines, thereby indicating utility, for example, in treating various anemias or for use in conjunction with irradiation/chemotherapy to

stimulate the production of erythroid precursors and/or erythroid cells; in supporting the growth and proliferation of myeloid cells such as granulocytes and monocytes/macrophages (i.e., traditional CSF activity) useful, for example, in conjunction with chemotherapy to prevent or treat consequent myelo-suppression; in supporting the growth and proliferation of megakaryocytes and consequently of platelets thereby allowing prevention or treatment of various platelet disorders such as thrombocytopenia, and generally for use in place of or complementary to platelet transfusions; and/or in supporting the growth and proliferation of hematopoietic stem cells which are capable of maturing to any and all of the above-mentioned hematopoietic cells and therefore find therapeutic utility in various stem cell disorders (such as those usually treated with transplantation, including, without limitation, aplastic anemia and paroxysmal nocturnal hemoglobinuria), as well as in repopulating the stem cell compartment post irradiation/chemotherapy, either in-vivo or ex-vivo (i.e., in conjunction with bone marrow transplantation or with peripheral progenitor cell transplantation (homologous or heterologous)) as normal cells or genetically manipulated for gene therapy.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for proliferation and differentiation of various hematopoietic lines are cited above.

Assays for embryonic stem cell differentiation (which will identify, among others, proteins that influence embryonic differentiation hematopoiesis) include, without limitation, those described in: Johansson et al. Cellular Biology 15:141-151, 1995; Keller et al., Molecular and

Cellular Biology 13:473-486, 1993; McClanahan et al., Blood 81:2903-2915, 1993.

Assays for stem cell survival and differentiation (which will identify, among others, proteins that regulate lympho-hematopoiesis) include, without limitation, those described in: Methylcellulose colony forming assays, Freshney, M.G. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 265-268, Wiley-Liss, Inc., New York, NY. 1994; Hirayama et al., Proc. Natl. Acad. Sci. USA 89:5907-5911, 1992; Primitive hematopoietic colony forming cells with high proliferative potential, McNiece, I.K. and Briddell, R.A. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 23-39, Wiley-Liss, Inc., New York, NY. 1994; Neben et al., Experimental Hematology 22:353-359, 1994; Cobblestone area forming cell assay, Ploemacher, R.E. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 1-21, Wiley-Liss, Inc., New York, NY. 1994; Long term bone marrow cultures in the presence of stromal cells, Spooner, E., Dexter, M. and Allen, T. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 163-179, Wiley-Liss, Inc., New York, NY. 1994; Long term culture initiating cell assay, Sutherland, H.J. In Culture of Hematopoietic Cells. R.I. Freshney, et al. eds. Vol pp. 139-162, Wiley-Liss, Inc., New York, NY. 1994.

#### Tissue Growth Activity

A protein of the present invention also may have utility in compositions used for bone, cartilage, tendon, ligament and/or nerve tissue growth or regeneration, as well as for wound healing and tissue repair and replacement, and in the treatment of burns, incisions and ulcers.

A protein of the present invention, which induces cartilage and/or bone growth in circumstances where bone is

not normally formed, has application in the healing of bone fractures and cartilage damage or defects in humans and other animals. Such a preparation employing a protein of the invention may have prophylactic use in closed as well as open fracture reduction and also in the improved fixation of artificial joints. De novo bone formation induced by an osteogenic agent contributes to the repair of congenital, trauma induced, or oncologic resection induced craniofacial defects, and also is useful in cosmetic plastic surgery.

10 A protein of this invention may also be used in the treatment of periodontal disease, and in other tooth repair processes. Such agents may provide an environment to attract bone-forming cells, stimulate growth of bone-forming cells or induce differentiation of progenitors of bone-forming cells. A protein of the invention may also be useful in the treatment of osteoporosis or osteoarthritis, such as through stimulation of bone and/or cartilage repair or by blocking inflammation or processes of tissue destruction (collagenase activity, osteoclast activity, etc.) mediated by inflammatory processes.

20 Another category of tissue regeneration activity that may be attributable to the protein of the present invention is tendon/ligament formation. A protein of the present invention, which induces tendon/ligament-like tissue or other tissue formation in circumstances where such tissue is not normally formed, has application in the healing of tendon or ligament tears, deformities and other tendon or ligament defects in humans and other animals. Such a preparation employing a tendon/ligament-like tissue inducing protein may have prophylactic use in preventing damage to tendon or ligament tissue, as well as use in the improved fixation of tendon or ligament to bone or other tissues, and

in repairing defects to tendon or ligament tissue. De novo tendon/ligament-like tissue formation induced by a composition of the present invention contributes to the repair of congenital, trauma induced, or other tendon or ligament defects of other origin, and is also useful in cosmetic plastic surgery for attachment or repair of tendons or ligaments. The compositions of the present invention may provide an environment to attract tendon or ligament-forming cells, stimulate growth of tendon- or ligament-forming cells, induce differentiation of progenitors of tendon- or ligament-forming cells, or induce growth of tendon/ligament cells or progenitors ex vivo for return in vivo to effect tissue repair. The compositions of the invention may also be useful in the treatment of tendinitis, carpal tunnel syndrome and other tendon or ligament defects. The compositions may also include an appropriate matrix and/or sequestering agent as a carrier as is well known in the art.

15 20 The protein of the present invention may also be useful for proliferation of neural cells and for regeneration of nerve and brain tissue, i.e. for the treatment of central and peripheral nervous system diseases and neuropathies, as well as mechanical and traumatic disorders, which involve degeneration, death or trauma to neural cells or nerve tissue. More specifically, a protein may be used in the treatment of diseases of the peripheral nervous system, such as peripheral nerve injuries, peripheral neuropathy and localized neuropathies, and central nervous system diseases, such as Alzheimer's, Parkinson's disease, Huntington's disease, amyotrophic lateral sclerosis, and Shy-Drager syndrome. Further conditions which may be treated in accordance with the present invention include mechanical and traumatic disorders, such as spinal cord disorders, head

trauma and cerebrovascular diseases such as stroke. peripheral neuropathies resulting from chemotherapy or other medical therapies may also be treatable using a protein of the invention.

6 Proteins of the invention may also be useful to promote better or faster closure of non-healing wounds, including without limitation pressure ulcers, ulcers associated with vascular insufficiency, surgical and traumatic wounds, and the like.

10 It is expected that a protein of the present invention may also exhibit activity for generation or regeneration of other tissues, such as organs (including, for example, pancreas, liver, intestine, kidney, skin, endothelium), muscle (smooth, skeletal or cardiac) and vascular (including vascular endothelium) tissue, or for promoting the growth of cells comprising such tissues. Part of the desired effects may be by inhibition or modulation of fibrotic scarring to allow normal tissue to regenerate. A protein of the invention may also exhibit angiogenic activity.

20 A protein of the present invention may also be useful for gut protection or regeneration and treatment of lung or liver fibrosis, reperfusion injury in various tissues, and conditions resulting from systemic cytokine damage.

25 A protein of the present invention may also be useful for promoting or inhibiting differentiation of tissues described above from precursor tissues or cells; or for inhibiting the growth of tissues described above.

The activity of a protein of the invention may, among other means, be measured by the following methods:

30 Assays for tissue generation activity include, without limitation, those described in: International Patent Publication No. WO95/16035 (bone, cartilage, tendon);

International Patent Publication No. WO95/05846 (nerve, neuronal); International Patent Publication No. WO91/07491 (skin, endothelium).

5 Assays for wound healing activity include, without limitation, those described in: Winter, Epidermal Wound Healing, pps. 71-112 (Maibach, HI and Rovee, DT, eds.), Year Book Medical Publishers, Inc., Chicago, as modified by Eaglestein and Mertz, J. Invest. Dermatol 71:382-84 (1978).

#### Activin/Inhibin Activity

10 A protein of the present invention may also exhibit activin- or inhibin-related activities. Inhibins are characterized by their ability to inhibit the release of follicle stimulating hormone (FSH), while activins and are characterized by their ability to stimulate the release of follicle stimulating hormone (FSH). Thus, a protein of the present invention, alone or in heterodimers with a member of the inhibin family, may be useful as a contraceptive based on the ability of inhibins to decrease fertility in female mammals and decrease spermatogenesis in male mammals.

15 Administration of sufficient amounts of other inhibins can induce infertility in these mammals. Alternatively, the protein of the invention, as a homodimer or as a heterodimer with other protein subunits of the inhibin- group, may be useful as a fertility inducing therapeutic, based upon the ability of activin molecules in stimulating FSH release from cells of the anterior pituitary. See, for example, United States Patent 4,798,885. A protein of the invention may also be useful for advancement of the onset of fertility in sexually immature mammals, so as to increase the lifetime reproductive performance of domestic animals such as cows, sheep and pigs.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

Assays for activin/inhibin activity include, without limitation, those described in: Vale et al., *Endocrinology* 91:562-572, 1972; Ling et al., *Nature* 321:779-782, 1986; Vale et al., *Nature* 321:776-779, 1986; Mason et al., *Nature* 318:659-663, 1985; Forage et al., *Proc. Natl. Acad. Sci. USA* 83:3091-3095, 1986.

#### Chemotactic/Chemokinetic Activity

A protein of the present invention may have chemotactic or chemokinetic activity (e.g., act as a chemokine) for mammalian cells, including, for example, monocytes, fibroblasts, neutrophils, T-cells, mast cells, eosinophils, epithelial and/or endothelial cells. Chemotactic and chemokinetic proteins can be used to mobilize or attract a desired cell population to a desired site of action. Chemotactic or chemokinetic proteins provide particular advantages in treatment of wounds and other trauma to tissues, as well as in treatment of localized infections. For example, attraction of lymphocytes, monocytes or neutrophils to tumors or sites of infection may result in improved immune responses against the tumor or infecting agent.

A protein or peptide has chemotactic activity for a particular cell population if it can stimulate, directly or indirectly, the directed orientation or movement of such cell population. Preferably, the protein or peptide has the ability to directly stimulate directed movement of cells. Whether a particular protein has chemotactic activity for a population of cells can be readily determined by employing such protein or peptide in any known assay for cell chemotaxis.

The activity of a protein of the invention may, among

other means, be measured by the following methods:

Assays for chemotactic activity (which will identify proteins that induce or prevent chemotaxis) consist of assays that measure the ability of a protein to induce the migration of cells across a membrane as well as the ability of a protein to induce the adhesion of one cell population to another cell population. Suitable assays for movement and adhesion include, without limitation, those described in: *Current Protocols in Immunology*, Ed by J.E. Coligan, A.M. Krulsbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 6.12, Measurement of alpha and beta Chemokines 6.12.1-6.12.28; Taub et al. *J. Clin. Invest.* 95:1370-1376, 1995; Lind et al. *APMIS* 103:140-146, 1995; Muller et al. *Eur. J. Immunol.* 25: 1744-1748; Gruber et al. *J. of Immunol.* 152:5860-5867, 1994; Johnston et al. *J. of Immunol.* 153: 1762-1768, 1994.

#### Hemostatic and Thrombolytic Activity

A protein of the invention may also exhibit hemostatic or thrombolytic activity. As a result, such a protein is expected to be useful in treatment of various coagulation disorders (including hereditary disorders, such as hemophilias) or to enhance coagulation and other hemostatic events in treating wounds resulting from trauma, surgery or other causes. A protein of the invention may also be useful for dissolving or inhibiting formation of thromboses and for treatment and prevention of conditions resulting therefrom (such as, for example, infarction of cardiac and central nervous system vessels (e.g., stroke)).

The activity of a protein of the invention may, among other means, be measured by the following methods:

Assay for hemostatic and thrombolytic activity include,

without limitation, those described in: Linet et al., J. Clin. Pharmacol. 26:131-140, 1986; Burdick et al., Thrombosis Res. 45:413-419, 1987; Humphrey et al., Fibrinolysis 5:71-79 (1991); Schaub, Prostaglandins 35:467-474, 1988.

#### Receptor/Ligand Activity

A protein of the present invention may also demonstrate activity as receptors, receptor ligands or inhibitors or agonists of receptor/ligand interactions. Examples of such receptors and ligands include, without limitation, cytokine receptors and their ligands, receptor kinases and their ligands, receptor phosphatases and their ligands, receptors involved in cell-cell interactions and their ligands (including without limitation, cellular adhesion molecules (such as selectins, integrins and their ligands) and receptor/ligand pairs involved in antigen presentation, antigen recognition and development of cellular and humoral immune responses). Receptors and ligands are also useful for screening of potential peptide or small molecule inhibitors of the relevant receptor/ligand interaction. A protein of the present invention (including, without limitation, fragments of receptors and ligands) may themselves be useful as inhibitors of receptor/ligand interactions.

The activity of a protein of the invention may, among other means, be measured by the following methods:

Suitable assays for receptor-ligand activity include without limitation those described in: Current Protocols in Immunology, Ed by J.E. Coligan, A.M. Kruisbeek, D.H. Margulies, E.M. Shevach, W. Strober, Pub. Greene Publishing Associates and Wiley-Interscience (Chapter 7.28, Measurement of Cellular Adhesion under static conditions 7.28.1-7.28.22),

Takai et al., Proc. Natl. Acad. Sci. USA 84:6864-6868, 1987; Bierer et al., J. Exp. Med. 168:1145-1156, 1988; Rosenstein et al., J. Exp. Med. 169:149-160 1989; Stoltenberg et al., J. Immunol. Methods 175:59-68, 1994; Stitt et al., Cell 80:661-670, 1995.

#### Anti-Inflammatory Activity

Proteins of the present invention may also exhibit anti-inflammatory activity. The anti-inflammatory activity may be achieved by providing a stimulus to cells involved in the inflammatory response, by inhibiting or promoting cell-cell interactions (such as, for example, cell adhesion), by inhibiting or promoting chemotaxis of cells involved in the inflammatory process, inhibiting or promoting cell extravasation, or by stimulating or suppressing production of other factors which more directly inhibit or promote an inflammatory response. Proteins exhibiting such activities can be used to treat inflammatory conditions including chronic or acute conditions), including without limitation inflammation associated with infection (such as septic shock, sepsis or systemic inflammatory response syndrome (SIRS)), ischemia-reperfusion injury, endotoxin lethality, arthritis, complement-mediated hyperacute rejection, nephritis, cytokine or chemokine-induced lung injury, inflammatory bowel disease, Crohn's disease or resulting from over production of cytokines such as TNF or IL-1. Proteins of the invention may also be useful to treat anaphylaxis and hypersensitivity to an antigenic substance or material.

#### Tumor Inhibition Activity

In addition to the activities described above for immunological treatment or prevention of tumors, a protein of the invention may exhibit other anti-tumor activities: A



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protein may inhibit tumor growth directly or indirectly (such as, for example, via ADCC). A protein may exhibit its tumor inhibitory activity by acting on tumor tissue or tumor precursor tissue, by inhibiting formation of tissues necessary to support tumor growth (such as, for example, by inhibiting angiogenesis), by causing production of other factors, agents or cell types which inhibit tumor growth, or by suppressing, eliminating or inhibiting factors, agents or cell types which promote tumor growth

#### 10 Other Activities

A protein of the invention may also exhibit one or more of the following additional activities or effects: inhibiting the growth, infection or function of, or killing, infectious agents, including, without limitation, bacteria, viruses, fungi and other parasites; effecting (suppressing or enhancing) bodily characteristics, including, without limitation, height, weight, hair color, eye color, skin, fat to lean ratio or other tissue pigmentation, or organ or body part size or shape (such as, for example, breast augmentation or diminution, change in bone form or shape); effecting biorhythms or circadian cycles or rhythms; effecting the fertility of male or female subjects; effecting the metabolism, catabolism, anabolism, processing, utilization, storage or elimination of dietary fat, lipid, protein, carbohydrate, vitamins, minerals, cofactors or other nutritional factors or component(s); effecting behavioral characteristics, including, without limitation, appetite, libido, stress, cognition (including cognitive disorders), depression (including depressive disorders) and violent behaviors; providing analgesic effects or other pain reducing effects; promoting differentiation and growth of

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embryonic stem cells in lineages other than hematopoietic lineages; hormonal or endocrine activity; in the case of enzymes, correcting deficiencies of the enzyme and treating deficiency-related diseases; treatment of hyperproliferative disorders (such as, for example, psoriasis); immunoglobulin-like activity (such as, for example, the ability to bind antigens or complement); and the ability to act as an antigen in a vaccine composition to raise an immune response against such protein or another material or entity which is cross-reactive with such protein.

#### 10 Examples

The present invention is specifically illustrated in more detail by the following Examples, but Examples are not intended to restrict the present invention. The basic operations with regard to the recombinant DNA and the enzymatic reactions were carried out according to the literature ["Molecular Cloning. A Laboratory Manual", Cold Spring Harbor Laboratory, 1989]. Unless otherwise stated, restrictive enzymes and a variety of modification enzymes to be used were those available from Takara Shuzo. The buffer compositions and the reaction conditions for each of the enzyme reactions were as described in the manufacturer's instructions. The cDNA synthesis was carried out according to the literature [Kato, S. et al., Gene 150: 243-250 (1994)].

#### 25 (1) Selection of cDNAs Encoding Proteins Having Hydrophobic Domains

The cDNA library of fibrosarcoma cell line HT-1080 (WO98/11217), the cDNA library of osteosarcoma cell line Saos-2 (WO97/33993), the cDNA library of osteosarcoma cell line U-2 OS (WO98/21328), the cDNA library of epidermoid

carcinoma cell line KB (WO98/11217), the cDNA library of tissues of stomach cancer delivered by the operation (WO98/21328), the cDNA library of liver tissue delivered by the operation (WO98/21328), and were used for the cDNA libraries. Full-length cDNA clones were selected from respective libraries and the whole base sequences thereof were determined to construct a homo-protein cDNA bank consisting of the full-length cDNA clones. The hydrophobicity/hydrophilicity profiles were determined for the proteins encoded by the full-length cDNA clones registered in the homo-protein cDNA bank by the Kyte-Doolittle method [Kyte, J. & Doolittle, R. F., J. Mol. Biol. 157: 105-132 (1982)] to examine the presence or absence of a hydrophobic region. Any clone that has a hydrophobic region being putative as a secretory signal or a transmembrane domain in the amino acid sequence of the encoded protein was selected as a clone candidate.

## (2) Protein Synthesis by In Vitro Translation

The plasmid vector bearing the cDNA of the present invention was used for in vitro transcription/translation with a T<sub>7</sub>T rabbit reticulocyte lysate kit (Promega). In this case, [<sup>35</sup>S]methionine was added to label the expression product with a radioisotope. Each of the reactions was carried out according to the protocols attached to the kit. Two micrograms of the plasmid was subjected to the reaction at 30°C for 90 minutes in the reaction solution of a total volume of 25  $\mu$ l containing 12.5  $\mu$ l of T<sub>7</sub>T rabbit reticulocyte lysate, 0.5  $\mu$ l of a buffer solution (attached to the kit), 2  $\mu$ l of an amino acid mixture (without methionine), 2  $\mu$ l of [<sup>35</sup>S]methionine (Amersham) (0.37 MBq/ $\mu$ l), 0.5  $\mu$ l of T7 RNA polymerase, and 20 U of RNasin. Also, an experiment in the presence of a membrane system was carried

out by adding to this reaction system 2.5  $\mu$ l of a canine pancreas microsome fraction (Promega). To 3  $\mu$ l of the resulting reaction solution was added 2  $\mu$ l of the SDS sampling buffer (125 mM Tris-hydrochloric acid buffer, pH 6.8, 120 mM 2-mercaptoethanol, 2% SDS solution, 0.025% bromophenol blue, and 20% glycerol) and the resulting mixture was heated at 95°C for 3 minutes and then subjected to SDS-polyacrylamide gel electrophoresis. The molecular weight of the translation product was determined by carrying out the autoradiography.

## (3) Expression by COS7

*Escherichia coli* cells bearing the expression vector for the protein of the present invention was incubated at 37°C for 2 hours in 2 ml of the 2xYT culture medium containing 100  $\mu$ g/ml of ampicillin, the helper phage M13KO7 (50  $\mu$ l) was added, and the incubation was continued at 37°C overnight. A supernatant separated by centrifugation underwent precipitation with polyethylene glycol to obtain single-stranded phage particles. These particles were suspended in 100  $\mu$ l of 1 mM Tris-0.1 mM EDTA, pH 8 (TE).

The cultured cells derived from simian kidney, COS7, were incubated at 37°C in the presence of 5% CO<sub>2</sub> in the Dulbecco's modified Eagle's culture medium (DMEM) containing 10% fetal calf serum. Into a 6-well plate (Nunc, well diameter: 3 cm) were inoculated with 1 x 10<sup>6</sup> COS7 cells and incubation was carried out at 37°C for 22 hours in the presence of 5% CO<sub>2</sub>. After the culture medium was removed, the cell surface was washed with a phosphate buffer solution and then washed again with DMEM containing 50 mM Tris-hydrochloric acid (pH 7.5) (TNMEM). To the resulting cells was added a suspension of 1  $\mu$ l of the single-stranded phage suspension, 0.6 ml of the DMEM culture medium, and 3  $\mu$ l of

TRANSFECTAM™ (IBF) and the resulting mixture was incubated at 37°C for 3 hours in the presence of 5% CO<sub>2</sub>. After the sample solution was removed, the cell surface was washed with TDWMEM, 2 ml per well of DMEM containing 10% fetal calf serum was added, and the incubation was carried out at 37°C for 2 days in the presence of 5% CO<sub>2</sub>. After the culture medium was replaced by a culture medium containing [<sup>35</sup>S]cysteine or [<sup>35</sup>S]methionine, the incubation was carried out for one hour. After the culture medium and the cells were separated by centrifugation, proteins in the culture medium fraction and the cell-membrane fraction were subjected to SDS-PAGE.

#### (4) Clone Examples

<HP01550> (SEQ ID Nos. 1, 11, and 21)

Determination of the whole base sequence of the cDNA insert of clone HP01550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 65-bp 5'-untranslated region, a 378-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 125 amino acid residues and there existed one putative transmembrane domain. Figure 1 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 15 kDa that was almost identical with the molecular weight of 13,825 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein F45G2.c (Genbank Accession No. 293382). Table 2 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C.

*elegans* hypothetical protein F45G2.c (CE). Therein, the marks of '-', '\*', and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.5% in the entire region.

Table 2

```

10  HP  MARYLAQITVGVGVGRAPARALRQEF-----AASRAAADARGRAGHSAAASNL-
      . . . . .
15  CE  MPNRTALKVLAAGENVAKALTRAVERDIRQOAAARHAASTGASSETRENANSNAKT
      HP  GLSLQEAQOITLVV-SKLSPEEVQKNVYELPKVNDKSVGGSFYLSKRVVAKERLDEEL-K
      * . . . . . * . . . . . * . . . . . * . . . . . * . . . . .
      CE  GISLESILQITLVKPEINREVERKHYELFNINDKSGGTYLSKRVVAKERLDEEFG
      HP  IQAQEDREKQMPHT
      * . . . . . * . . . . . * . . . . . * . . . . . * . . . . .
      CE  IELKEKKKENNAKTE

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Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA338859) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02593> (SEQ ID Nos. 2, 12, and 22)

Determination of the whole base sequence of the cDNA insert of clone HP02593 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 103-bp 5'-untranslated region, a 396-bp ORF,



present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 46.5% in the entire region.

Table 4

```

HP MAHEQILVLDPTDLKFGPTDVVTNLKLNPSDRKVCVKITDAPRYCVRNPSGI
*****
AP MASHBQALIEPAGELARFGPTDVVTADLKLSNPTDRICFVKTAPKRYCVRNPSGI
HP IDGSTVTVSVMLQFPDYDPNEKSKHKFNVQITFADPTSD--MEAVKTEARPELDLSKL
*****
AP LEPKTSIAVAVMLQFPDYDPNEKSKHKFNVQSMADPHVESQELLMKADPESLMDTKL
HP RCVFEPNPNNDKLNDEPSK-----AVPLNASKODGPRKP--HVSILNDTE
*****
AP RCVFEPNPNNDKLNDEPSK-----AVPLNASKODGPRKP--HVSILNDTE
HP RCVFEPNPNNDKLNDEPSK-----AVPLNASKODGPRKP--HVSILNDTE
*****
AP RCVFEPNPNNDKLNDEPSK-----AVPLNASKODGPRKP--HVSILNDTE
HP TRIMAECKRIQGEWKLSEENRHLRDEGLRIRKVAHSD--KPGSTSTASFRDNTSPLP
*****
AP VKLQHELKKAQSEITSLKGENSQLKDEGIRLRKVAHSD--KPGSTSTASFRDNTSPLP
HP SLIVTIAAIFIGFLGKFTL
...
AP PVYVVAALIIIGLIGKFTL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA447905) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10423> (SEQ ID Nos. 4, 14, and 24)

Determination of the whole base sequence of the cDNA insert of clone HP10423 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure consisting of a 64-bp 5'-untranslated region, a 795-bp ORF, and a 207-bp 3'-untranslated region. The ORF codes for a protein consisting of 264 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the N-terminus. Figure 4 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 30 kDa that was almost identical with the molecular weight of 29,377 predicted from the ORF. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D80116) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10506> (SEQ ID Nos. 5, 15, and 25)

Determination of the whole base sequence of the cDNA insert of clone HP10506 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 53-bp 5'-untranslated region, a 339-bp ORF, and a 226-bp 3'-untranslated region. The ORF codes for a protein consisting of 112 amino acid residues and there existed one putative transmembrane domain. Figure 5 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-

Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,821 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282544) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

15 <HP10507> (SEQ ID Nos. 6, 16, and 26)

Determination of the whole base sequence of the cDNA insert of clone HP10507 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 412-bp 5'-untranslated region, a 441-bp ORF, and a 168-bp 3'-untranslated region. The ORF codes for a protein consisting of 146 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 6 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 16,347 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10548> (SEQ ID Nos. 7, 17, and 27)

Determination of the whole base sequence of the cDNA insert of clone HP10548 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 330-bp 5'-untranslated region, a 1035-bp ORF, and a 67-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed four putative transmembrane domains. Figure 7 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of a high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA143152) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10566> (SEQ ID Nos. 8, 18, and 28)

Determination of the whole base sequence of the cDNA insert of clone HP10566 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 61-bp 5'-untranslated region, a 294-bp ORF, and a 246-bp 3'-untranslated region. The ORF codes for a protein consisting of 97 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 8 depicts the

hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,452 predicted from the ORF. When expressed in COS7 cells, an expression product of about 12 kDa was observed in the membrane fraction.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W79821) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

15 <HP10567> (SEQ ID Nos. 9, 19, and 29)

Determination of the whole base sequence of the cDNA insert of clone HP10567 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 77-bp 5'-untranslated region, a 375-bp ORF, and a 133-bp 3'-untranslated region. The ORF codes for a protein consisting of 124 amino acid residues and there existed one putative transmembrane domain at the C-terminus. Figure 9 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 14 kDa that was almost identical with the molecular weight of 14,484 predicted from the ORF.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA428475) in ESTs, but, since they

are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

5 <HP10568> (SEQ ID Nos. 10, 20, and 30)

Determination of the whole base sequence of the cDNA insert of clone HP10568 obtained from cDNA library of the human stomach cancer revealed the structure consisting of a 56-bp 5'-untranslated region, a 984-bp ORF, and a 60-bp 3'-untranslated region. The ORF codes for a protein consisting of 327 amino acid residues and there existed a secretory signal at the N-terminus and one putative transmembrane domain at the C-terminus. Figure 10 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36.5 kDa that was almost identical with the molecular weight of 34,326 predicted from the ORF. In this case, the addition of a microsomal led to the formation of a product of 40 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Leu-Thr at position 138 and Asn-Leu-Ser at position 206). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from valine at position 24. When expressed in COS7 cells, an expression product of about 31 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein has revealed that the protein was similar to the human cell-surface A33 antigen

(SWISS-PROT Accession No. Q99795). Table 5 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human cell-surface A33 antigen (A3). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.0% in the N-terminal region of 243 residues.

Table 5

[illegible]

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

of sequences that shared a homology of 90% or more (for example, Accession No. T24595) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01426> (SEQ ID Nos. 31, 41, and 51)

Determination of the whole base sequence of the cDNA insert of clone HP01426 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 1-bp 5'-untranslated region, a 942-bp ORF, and a 122-bp 3'-untranslated region. The ORF codes for a protein consisting of 313 amino acid residues and there existed a putative secretory signal. Figure 11 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 34,955 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 38 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ser-Ser at position 163). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from tryptophan at position 17. When expressed in COS7 cells, an expression product of about 39 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the



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protein was similar to the *Xenopus laevis* cortical granule lectin (EMBL Accession No. X82628). Table 6 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the X. laevis cortical granule lectin (XL). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 67.9% in the region other than the N-terminal region.

Table 6

[illegible]

56

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R06009) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02515> (SEQ ID NOS. 32, 42, and 52)

10 Determination of the whole base sequence of the cDNA  
insert of clone HPO2515 obtained from cDNA library of human  
osteosarcoma cell line Saos-2 revealed the structure  
consisting of a 176-bp 5'-untranslated region, a 690-bp ORF,  
and a 71-bp 3'-untranslated region. The ORF codes for a  
protein consisting of 229 amino acid residues and there  
existed a putative secretory signal at N-terminus and one  
putative transmembrane domain at the C-terminus. Figure 12  
depicts the hydrophobicity/hydrophilicity profile, obtained  
by the Kyte-Doolittle method, of the present protein. In  
vitro translation resulted in formation of a translation  
product of 27 kDa that was almost identical with the  
molecular weight of 26,000 predicted from the ORF. In this  
case, the addition of a microsome led to the formation of a  
product of 25.5 kDa from which the secretory signal is  
considered to have been cleaved. Application of the (-3,-1)  
rule, a method for predicting the cleavage site of the  
secretory signal sequence, allows to expect that the mature  
protein starts from phenylalanine at position 28.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human T1/S72 receptor binding protein (GenBank Accession No. U41804). Table 7 shows the

comparison between amino acid sequences of the human protein of the present invention (HP) and the human T1/ST2 receptor binding protein (T1). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 55.8% in the entire region.

Table 7

```
HP  MGDKIWLPPVLLAALPPVLLPAGAGFTPSLSDSFTFTLPAGQKECFYQPHPLKASLE
      ..... * * * * * * * * * * * * * * * * * * * * * * * * * * * *
T1  MMAAGAALALALWLL--HPPVEV--GGAGPPIDGGEFTFLPAGRKQCFYOSAPANASLE
HP  IEYQVLGAGLDIDFHLASPEGKTLVFEQRKSDGVHTVE--TEVGDYMFCEPNTFTISEK
      ..... * * * * * * * * * * * * * * * * * * * * * * * * * * * *
T1  TEYQVIGGAGLDVDFLESPOGVLLVSESRKADGVHTVEPTAGDYKLCFDPNSFTISEK
HP  VIFFELIDNNGEQAEQZDMKKYITGTDILDMKLEDILESINSIKRSLKSGHIQILLR
      ..... * * * * * * * * * * * * * * * * * * * * * * * * * * * *
T1  LVPFELIFDSL-QDDEVEVGMAEAVEPEEMLDVNMEDIKESIETMRTLERSIQMLTLAR
HP  AFEARDNIGESNFDVNFNSHVLNVVVVWSAIVYMLKSLFEDKRSRT
      ..... * * * * * * * * * * * * * * * * * * * * * * * * * * * *
T1  AFEARDNLQEGNLERNVFNWSAVNVAVLLELVAVLQVCTLKRFFQDRPVPT
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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA381943) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02575> (SEQ ID Nos. 33, 43, and 53)

Determination of the whole base sequence of the cDNA insert of clone HP02575 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1404-bp ORF, and a 219-bp 3'-untranslated region. The ORF codes for a protein consisting of 467 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 13 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 52 kDa that was almost identical with the molecular weight of 54,065 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 57 kDa which is considered to have a sugar chain being attached after secretion. In addition, there exist in the amino acid sequence of this protein three sites at which N-glycosylation may occur (Asn-Arg-Thr at position 171, Asn-Ser-Thr at position 239 and Asn-Asp-Thr at position 377). Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from histidine at position 29. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human  $\alpha$ -L-fucosidase (SWISS-PROT Accession No. P04066). Table 8 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human  $\alpha$ -L-fucosidase (FC). Therein,



insert of clone HP10447 obtained from cDNA library of human liver revealed the structure consisting of a 271-bp 5'-untranslated region, a 570-bp ORF, and a 34-bp 3'-untranslated region. The ORF codes for a protein consisting of 189 amino acid residues and there existed five putative transmembrane domains. Figure 15 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA296976) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

**<HP10477> (SEO ID Nos. 36, 46, and 56)**

Determination of the whole base sequence of the cDNA insert of clone HPI0477 obtained from cDNA library of human liver revealed the structure consisting of a 149-bp 5'-untranslated region, a 1092-bp ORF, and a 15-bp 3'-untranslated region. The ORF codes for a protein consisting of 363 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 16 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39.884 predicted from the ORF.

The search of the protein data base using the amino

acid sequence of the present protein revealed that the protein was similar to the human peptidoglycan recognition protein (GenBank Accession No. AF076483). Table 9 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human peptidoglycan recognition protein (PG). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 54.8% in the entire region.

Table 9

```

15  HP MVDSLAVTIAGNLGTLFURGSOTQSHDPDLGTGECWQDLSAPRTFTLLDPKASLTLKFTFL
    HP NGALDGYILGDIYSRTPEPRLSHLLSQYVGAGVARDPGRSFRNQGAALTSASILA
    HP QOVWGTILVLQRLPEVHLQLOCMQSOQLAAVNAATKEFTEAFLGCPAIFHCRCWGAAPY
      * * * * *
20  PG MSRRSMLLAWALLPSLLRLGAQAQETEDPACCSPIVPRNEWKALA-
    HP RGRPKLLQLPLGLFYVHHYTVZAPPCTDFTRCANMRSQMRYHODTQGWGDIGYSFVVG
      * * * * *
    PG SECAOHLSLFLRYVVVWST--AGSSCNTPASQOQOARNVQHYHMKILGWCDVGVNFIIGE
    HP DGVYEGRGWHWVGAAHTLGH-NSRFGVAIVGNYTAALPTEAALRTVRDILPSCAVRAGL
      * * * * *
    PG DGLVYEGRGWNETGAHSGHLNPNMSIGISPMGNTHDRVPTFOAIRAAQGLL-ACGVAQGA
    HP LRPDYALLGHQRLVTRDCPGOALFDLLRTNPHFTATVKPRPARSVKRSRREPPPTLPA
      * * * * *
    PG LRSNVYKGRHVDORTLSPGNQLYHLIQNWPYHRSF

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration

of sequences that shared a homology of 90% or more (for example, Accession No. AA424759) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10513> (SEQ ID Nos. 37, 47, and 57)

Determination of the whole base sequence of the cDNA insert of clone HP10513 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 134-bp 5'-untranslated region, a 750-bp ORF, and a 0-bp 3'-untranslated region. The ORF codes for a protein consisting of 249 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 17 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 27,373 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0512 (GenBank Accession No. AB011084). Table 10 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0512 (KI). Therein, the marks of \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 31.6% in the C-terminal region of 196 amino acid residues.

Table 10

HP	MGGPRGAGVVAAGLLGAGACYCIVRLTRGRRG
5	
10	KI RGRGRPVVAQKRPPEYIEIDELIGVRDLKRVALLQKSDDPFIQQVALLTSSNNANYSN HP DRELGINSSKSAEDLTGSDYDVLAHQKLLYLLESTEDPVITIERALITLGNNAFSAV * ..... * KI QETIRKLGELPIIANMINKTDPHIKEKALMAANNLSSEVENQGRQLQVYKXVMDIMASN HP NQAIIRRELGIPIVANKINHSNQSIKAKALNALNLSVVENQIKIKVQVLKLLNLSEN * ..... * KI LNSAVQVVGKFTNTMTNDYQHLVNSIANF--FRLLSQGGKIKVILKILSLFAFN HP PMTEGLLRAQVDSFSLYDSHVAKKELLRLVTLFQNIKNCIXGHILAVQPTPEGSL * ..... * KI PDLKRLISTQVPASFSLYNSVSESLINALTPEIITDNLRAE--VFNTYRFPKGSIL HP FFL-LNGECAQKIRALVDHDAVKEKVVITIPKI * ..... * KI FYLCITTSQVCVKIRALNHHDLVKKVYIKLVNKF
15	
20	
25	
30	

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N92228) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10540> (SEQ ID Nos. 38, 48, and 58)

Determination of the whole base sequence of the cDNA insert of clone HP10540 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure

consisting of a 47-bp 5'-untranslated region, a 297-bp ORF, and a 245-bp 3'-untranslated region. The ORF codes for a protein consisting of 98 amino acid residues and there existed two putative transmembrane domains. Figure 18 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CEF49C12.12 (GenBank Accession No. Z68227). Table 11 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CEF49C12.12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 36.1% in the entire region.

Table 11

25	HP M-ASLLCCGPKLAACGVLSANGVIMLMIGIFPNVHSAVLIEDVPFTEKDFENGPNQIY
	*        ***    *    *    *    *    *    *    *    *    *    *    *
	CE MGKICPLMGPKMSAFNCWHSVWGVIYELGLLGVFFIYQAVTLFEDLHF-EGHGKVPSSVID
	HP NLYEQVSYNCFIAAGLYLLGGFSPCQVRLNKRKEYMVR
	*        *        *        *        *
30	CE AKYNEKATQCIWIAAGLYAVTLIAVFWQ---NKYNTAQIF

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA420715) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

10 <HP10557> (SEQ ID Nos. 39, 49, and 59)

Determination of the whole base sequence of the cDNA insert of clone HP10557 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 24-bp 5'-untranslated region, a 519-bp ORF, and a 130-bp 3'-untranslated region. The ORF codes for a protein consisting of 172 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 19 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 32 kDa that was larger than the molecular weight of 18,844 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 39 kDa which is considered to have been subjected to some modification after secretion. In addition, there exist in the amino acid sequence of this protein no site at which N-glycosylation may occur. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 32. When expressed in COS7 cells, an expression product of about 20 kDa was observed in the supernatant fraction and the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human progesterone binding protein (EMBL Accession No. AJ002030). Table 12 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human progesterone binding protein (PG). Therein, the marks of '-', '\*', and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 30.5% in the C-terminal region of 151 amino acid residues.

Table 12

15	HP	PG
	HP	PG
	MAAGDGVKLTGSGSESSNDGSESPGDAGAAAGGNAALALITGGEMLNVAL	MAAGDGVKLTGSGSESSNDGSESPGDAGAAAGGNAALALITGGEMLNVAL
	HP RRLRLPLAALALVLAAPGLPTARAGTPPARRCPPV--RLFTEELARYGGEEDQPI	HP RRLRLPLAALALVLAAPGLPTARAGTPPARRCPPV--RLFTEELARYGGEEDQPI
	PG VALVILGAYRLVMWNRRLGAGAGAGEESPATSLPRMKRDFSLQLRQYDG-SRNPRI	PG VALVILGAYRLVMWNRRLGAGAGAGEESPATSLPRMKRDFSLQLRQYDG-SRNPRI
	HP YLAIRGVVFDVTSKGKPYGRGAPYNALTKRDSRGVAKSLDPADLTHTDTGILTAKELEA	HP YLAIRGVVFDVTSKGKPYGRGAPYNALTKRDSRGVAKSLDPADLTHTDTGILTAKELEA
	PG LLAVNGKVFDTGSKPYGRGAPYGFAGRDASRGLATPCLDKALRDEYDLSDLNVAQ	PG LLAVNGKVFDTGSKPYGRGAPYGFAGRDASRGLATPCLDKALRDEYDLSDLNVAQ
	HP LDEV--FTKVKYKAKYPIYGYTARILNEDSPNLDKPEDQPHDIKDER	HP LDEV--FTKVKYKAKYPIYGYTARILNEDSPNLDKPEDQPHDIKDER
	PG MESVREMEMQEKYK--DIYG-RLIKRGEEPS-EYTDDEEDTRDNHKKOD	PG MESVREMEMQEKYK--DIYG-RLIKRGEEPS-EYTDDEEDTRDNHKKOD

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for

example, Accession No. AA101709) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10563> (SEQ ID Nos. 40, 50, and 60)

Determination of the whole base sequence of the cDNA insert of clone HP10563 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 126-bp 5'-untranslated region, a 363-bp ORF, and a 936-bp 3'-untranslated region. The ORF codes for a protein consisting of 120 amino acid residues and there existed two putative transmembrane domains. Figure 20 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 18.5 kDa that was larger than the molecular weight of 13,180 predicted from the ORF.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Arabidopsis thaliana hypothetical protein F27F23.15 (Genbank Accession No. AC003058). Table 13 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the A. thaliana hypothetical protein F27F23.15 (AT). Therein, the marks of '-', '\*', and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.5% in the entire region.









osteosarcoma cell line Saos-2 revealed the structure consisting of a 61-bp 5'-untranslated region, a 672-bp ORF, and a 384-bp 3'-untranslated region. The ORF codes for a protein consisting of 223 amino acid residues and therefore existed a putative secretory signal at the N-terminus. Figure 24 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 27 kDa that was somewhat larger than the molecular weight of 24,555 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 26 kDa from which the secretory signal is considered to have been cleaved. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glutamine at position 20.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse FGF binding protein (Genbank Accession No. U49611). Table 17 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse FGF binding protein (MM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 21.2% in the entire region other than the N-terminal region. In particular, all the eight cysteine residues contained in the both proteins were conserved.

Table 17

[illegible]

20 Furthermore, the search of the GenBank using the base  
sequences of the present cDNA has revealed the registration  
of sequences that shared a homology of 90% or more (for  
example, Accession No. AA317400) in ESTs, but, since they  
are partial sequences, it can not be judged whether or not  
25 any of these sequences codes for the same protein as the  
protein of the present invention.

<HP02631> (SEQ ID NOS. 65, 75, and 85)

Determination of the whole base sequence of the cDNA insert of clone HPD2631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 147-bp ORF,

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and a 1191-bp 3'-untranslated region. The ORF codes for a protein consisting of 48 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 25 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa or less.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. A156969) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02632> (SEQ ID Nos. 66, 76, and 86)

Determination of the whole base sequence of the cDNA insert of clone HP02632 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 50-bp 5'-untranslated region, a 1116-bp ORF, and a 337-bp 3'-untranslated region. The ORF codes for a protein consisting of 371 amino acid residues and there existed eight putative transmembrane domains. Figure 26 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELC2H12 (GenBank Accession No. U23169). Table 18 shows the comparison between amino acid sequences

of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CELC2H12 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 51.4% in the entire region.

Table 18

10	HP	MAWTKYQLFLAGLMLVTGSIINTLSAKWADFNFAEGCGGSKHSFQHPFLQAVGNFLGFS
	CE	KVAFVAVIISVMVVTGSIINTICAKWADSIKAD-----GVFFNHPFLQATCFHFGSFL
	HP	CLAAPYL-----LRCAAGQSDS-----SVDPQQPFNPLFLPPALCDHGTSL
15	HP	CLVYFFLIFGKRYVNRANVGSGSVTEITSEKPLPFNFPLFPFPALCDILGTSI
	HP	MYVALNWTSSSFQMLRGAVIIFTGLSVGLMNAQIKFKWFGMLFVNLGLVIVGVTDIY
20	HP	SKHDSQHLSEVITCDLLIINAQIIIVAIQWLEKRVYKHNVHPLRAVGTGLFGFVLS
	HP	YDDPDLDDKNVITGNLLIWAQIIIVAIQWYEQYLTKYDVPALFAVGLGLFGMTLS
25	HP	LLVPMYIIPAG-SFSGNPRGTLEDALDAPCQVQCPQLIAVALLGNISSIAFFNFAGISV
	HP	ILMIPFYIHVPRTFTNPEGRLEDVFIYANKEITEPTIALALSGTVVSIAFFNFAGVSV
	HP	TKELSATRRVLDLSRTVIVWVSIPLFHEKFIQISGFAMLIIGTLIYNDIIGWFR
30	HP	LSRGRPLAESEQRLLGGTRTPINDAS
	HP	RNLLPNLSSHANCARCWLCICGGDSELIYEVEQDEHLNEA

79

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. N50907) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10488> (SEQ ID Nos. 67, 77, and 87)

Determination of the whole base sequence of the cDNA insert of clone HP10488 obtained from cDNA library of human liver revealed the structure consisting of a 39-bp 5'-untranslated region, a 273-bp ORF, and a 421-bp 3'-untranslated region. The ORF codes for a protein consisting of 90 amino acid residues and there existed one putative transmembrane domain at the N-terminus. Figure 27 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,151 predicted from the ORF. When expressed in COS7 cells, an expression product of about 6 kDa was observed in the membrane fraction.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H73534) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10538> (SEQ ID Nos. 68, 78, and 88)

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Determination of the whole base sequence of the cDNA insert of clone HP10538 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 357-bp 5'-untranslated region, a 1500-bp ORF, and a 1911-bp 3'-untranslated region. The ORF codes for a protein consisting of 499 amino acid residues and there existed at least four putative transmembrane domains. Figure 28 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the mouse pore-forming K<sup>+</sup> channel subunit (GenBank Accession No. AF056492). Table 19 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the mouse pore-forming K<sup>+</sup> channel subunit (MM). Therein, the marks of '-', '\*', and '·' represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 32.4% in the N-terminal region of 241 amino acid residues.





which is considered to have a sugar chain being attached after secretion. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Ile-Thr at position 10).

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA105822) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP01470> (SEQ ID Nos. 91, 101, and 111)

Determination of the whole base sequence of the cDNA insert of clone HP01470 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 157-bp 5'-untranslated region, a 1077-bp ORF, and a 385-bp 3'-untranslated region. The ORF codes for a protein consisting of 358 amino acid residues and there existed one putative transmembrane domain. Figure 31 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 43 kDa that was somewhat larger than the molecular weight of 40,489 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 40 kDa from which the secretory signal is considered to have been cleaved and a product of 43.5 kDa which is considered to have been subjected to some modification. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 23. When

expressed in COS7 cells, an expression product of about 44 kDa was observed in the supernatant fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein 39.9 kDa (SWISS-PROT Accession No. Q10005). Table 20 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein 39.9 kDa (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 58.9% in the entire region.

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Table 20

HP MAPQNLSTFCILLLYLIGAVIAGRDFYKILGVPRASIKDKKAYRKLALQLHPRNPD  
5  
CE MRLNVSLLVASSLVAFCGRDFVKILGVAKNANANQIKKAYRKLAKELHPRNQDD  
HP POAQRQDLGAAVEVLSDEKRRKQYDTYGEGL--KQGHQSSHGDISSHFFGDFGTFPG  
CE EMANEKFDLSSAYEVLSDKEKRAMYDRHGEAGVAKMGGGGGGHDPSFFSGDP-FG-G  
HP GTRQQRNIPRGSDIIVDLVLEEVYAGNFVVRNKPVARQAPGRKCNCEQEMRTT  
10  
CE GGGHGGEGTPKADVTIDLVLEEVYNGHFVLEIKRKAVYKQTSGRQNCHEHRT  
HP QLGPRFQMTQEVVCECPNVLNERTLEVEIEPCVRDGEYFFICEGEPHVDGEPGD  
CE QMGQGRFQMFQVQVCECPNVLQENKLVLEVEVEVGADNGHQIIFHGECEPHIEGDPGD  
HP LRFRIVVVRKPIFERRGDDLYTNVTSLVESLVGFEMDITHLDGKHVHSRDKITRPGAK  
CE LKFKIRIQKHPRTERKGDLYTNVTSIQDALNGFEMEIOHLDGHIUVQDRKVTWPGAR  
HP LWRKGEGLPNFNNIKSLIITFDVDPPEKQTEAREGIKQLLKQSSVQ-KVYNGLQC  
20  
CE LRKKDGMPSLEDNNKKGMLVTFDVEFPKTELSDEQAQIIEILQONTVPRAYNGL

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA282838) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

30 <HP002419> (SEQ ID Nos. 92, 102, and 112)

Determination of the whole base sequence of the cDNA insert of clone HP02419 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 253-bp

5'-untranslated region, a 681-bp ORF, and a 1120-bp 3'-untranslated region. The ORF codes for a protein consisting of 226 amino acid residues and there existed four putative transmembrane domains. Figure 32 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human hypothetical protein KIAA0108 (SWISS-PROT Accession No. Q15012). Table 21 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human hypothetical protein KIAA0108 (KI). Therein, the marks of \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 43.9% in the entire region.

Table 21

```

5  HP MKKVAPEWTRFYSNCCLCCHVTRGTILGWIYLIINAVVLLILSLADPD---QY
      *****
      KI MYSNSFKRNRSDRYSSTRCGCCCHVTRGTITLIGWYVWVLLMALITVEVTHPSNNAV
      HP NFSSEIAGDFEF-MDDANMCIALAISLMLICAMATGAYKQRAWIIFFCQIDF
      * . . . . . * . . . . . * . . . . . * . . . . . * . . . . . *
      KI NIQEVIGNYYSSERMADNACVLEFASVLMFTISSMLVGAISYQVGMIIFFCRLDF
      HP ALNMLVATVLIYFNSIOEYIRQLPPNFPRYRDVMSVNPCLVLIILFTISILFFKGYL
      * . . . . . * . . . . . * . . . . . * . . . . . * . . . . . *
      KI VLSCIVAISSITVLPRIKEYLDQL-PDFPYKDDLALDSSCLLFIVLVFPALFIIFKAYL
      HP ISCVNRCYRYINGRSSDVLVYVYV-SNDTIVLLPPYDADFVNGANAPPPYVSA
      * . . . . . * . . . . . * . . . . . * . . . . . * . . . . . *
      KI INCVMNCKYKINNNVPEIAVYPAFAPQVYLPYV-EMAVKMEKEPPPYLPA

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Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA173214) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

20

25 <HP02631> (SEQ ID Nos. 93, 103, and 113)

Determination of the whole base sequence of the cDNA insert of clone HP02631 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 42-bp 5'-untranslated region, a 588-bp ORF, and a 750-bp 3'-untranslated region. Although the 49th amino acid residue is encoded by a stop codon, it is likely that this codon encodes selenocysteine from the molecular weight

30

of the translation product and the sequence comparison data with the *Caenorhabditis elegans* homologue. The ORF codes for a protein consisting of 195 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 33 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 58 kDa. In this case, the addition of a microsome led to the formation of a product of 56 kDa from which the secretory signal is considered to have been cleaved. Since both of these products are larger than the molecular weight of 22 kDa predicted from the ORF, it is likely that the protein interacts with another protein.

15

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein C35C5.3 (EMBL Accession No. Z78417). Table 22 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein C35C5.3 (CE). U at position 49 in the amino acid sequence of the protein of the present invention represents selenocysteine. Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.9% in the entire region other than the N-terminal region. Cysteine was found in the sequence of the *C. elegans* protein at the position corresponding to position 49 encoded by the stop codon (selenocysteine) of the protein of the present invention.

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20

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Table 23

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5 HP MNELLIMLLVLCALLLLVQLRFLRADGDTLMAENQGRREPELTDVAVVTGASS
HP GIGELAYQLSKLGSLVLSARRVHELKRCLENGNLKEDLVLPDLDTGSHEA
*****
RN VKRSLKENGNLKEDLVLPDLADTSSHDI
HP ATKAVLQEPGRIDILVNGGMSQSRSLCMQTSIDVTRKLIENLYGTVSLTKCVLPHMER
*****
10 RN ATKVTLQEPGRIDILVNGGVAHASIVENTNDIFKVLIEVNYLGTVSLTKCVLPHMER
HP KQGRIVTVNSIIIGIISVPLISIGYCAKHALRGFENGLRTELATYFGIIVSNICPGPVQSN
*****
RN NQGRIVVMKS

```

16 Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. T84331) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 <HP10031> (SEQ ID Nos. 95, 105, and 115)

Determination of the whole base sequence of the cDNA insert of clone HP10031 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1464-bp ORF, and a 649-bp 3'-untranslated region. The ORF codes for a protein consisting of 487 amino acid residues and there existed eleven putative transmembrane domains. Figure 35 depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. When expressed in COS7 cells, an expression product of about 55 kDa was observed in the membrane fraction.

5 The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein CELK07H8 (GenBank Accession No. AF047659). Table 24 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein CELK07H8 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 44.2% in the entire region.





human protein of the present invention (HP) and the A. thaliana hypothetical protein IG002N01 (AT). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 27.0% in the N-terminal region of 355 amino acid residues.

Table 25

HP	MTLFLNLML
5	AT MEITSPQSPSSNDVSESVSVNMSMRARRSSAASLKRNDGYESLCQVYQODSDR HP ALACSPVHTTSLKSDAKAASKTLEKSQSDKRVQGRGLVVDLKRESVLEHRSYCSA .....*
10	AT LITIVFFIVIPAVSIAYVKFADNVIQTESSIRQKGIKXIDINQELITEHSK--AS HP KADRRFAGDVLGYVTPNNSHGVDVTVFGSKTQISPVNLQ-LKRGGRNPEVTGLNDV .....*
15	AT ENSTRHYDYPVLAITP--CQSGEL--VLEGR-HNADKGIQELRSKGNLSASKGLPKL HP DQGMRAVAKKAKGLHIVPRLLFEDWTYDPRNVLDSEDEIEELSKTVQVAKKQHFDF .....*
20	AT ---YNSCIFALKRMNFFTELVNENTYLVIMEALNS-REMEYNGIVLESMSRHAAYGVL HP VVEVNNQLSQKRVGLIMLTPLALHQAALLVIPALITPGDQLGNFTKKEPEQL .....*
25	AT HBDLAKMALKFVKQLGDALHSTSSPRNNQHMQPMYVVGPPRSEKLOMTDPGEDIQFL HP APVLDFSLMTYDVSTAHQPGNNAPLSWRAVQV-VLDPSK---WRSKILLGLNFGM *****
30	AT KDSVDGFSIMTYDFSNPQPGNAPVKWIDLTTLKLLGSSNNIDSNIAKRVLLGINFYN HP DVATSKDAREPVGARVITQLKDRPRWVWDSQASEHFPEYKKSRSRGHVVFPYTLKSLQ *****
35	AT DFVTSGGGGGATGRDYLLALQKHKPTFRMDKESGEHLFWYRQDNKIKHVAFFYPTLMSIL HP VRLLEARELGVSIMELGGGLDYFDLL *****
40	AT LRLNARLWIGIGISIMEIGDKGHFGKYAEASLEASSIFSGHTFPDMQFRTPNROLSHNGS .....*

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA302913) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the

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protein of the present invention.

<HP10541> (SEQ ID Nos. 97, 107, and 117)

Determination of the whole base sequence of the cDNA insert of clone HP10541 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 7-bp 5'-untranslated region, a 591-bp ORF, and a 113-bp 3'-untranslated region. The ORF codes for a protein consisting of 196 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 37 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat larger than the molecular weight of 21,553 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of 20 kDa from which the secretory signal is considered to have been cleaved and a product of 23 kDa which is considered to have a sugar chain being attached. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from glycine at position 41. In addition, there exists in the amino acid sequence of this protein one site at which N-glycosylation may occur (Asn-Leu-Thr at position 185).

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human zymogen membrane protein (GenBank Accession No. AF056492). Table 26 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human zymogen membrane protein (2M). Therein, the marks of -, \*, and . represent a

gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 37.6% in the C-terminal region of 133 amino acid residues.

Table 26

10	HP	MRVPGTTRPVTGESPCGHRPEAMILLLLTLLGGLTGWAGKMYGPGGKGYFS-TTEDVD	..*****
20	2M	MLTVALLALCASAGNAIQARSSSYSGEYSGGGKRRFSHSGNQILD	
HP	HBITGLRVSGLLLVKSVQVKLGSDWVKLGALGGNTQEVTLQPGYITKVFVAFQAFLR	..*****	
15	2M	GPITALRVRVNTYYIVGLQVRYGRVSDYVGGKNGDLEIFLHPGESVIOVSGKVKWYIK	
HP	GMWYTSKDRYFYFGKLDGQISSAYPSQEGQVLGVYGVQLLGKISIGFEWN-YPLERP	..*****	
20	2M	KLVFTDKRYLSFGKDSGTSFNAVPLHPNTVLRPFISGRSGSL-IDAIGLHWDVYPTSCS	
HP	TTEPPVNIYTSANSFVGR		

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA340605) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10550> (SEQ ID Nos. 98, 108, and 118)

Determination of the whole base sequence of the cDNA

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Insert of clone HP10550 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 241-bp 5'-untranslated region, a 324-bp ORF, and a 86-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 38 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA348310) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10590> (SEQ ID Nos. 99, 109, and 119)

Determination of the whole base sequence of the cDNA insert of clone HP10590 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 77-bp 5'-untranslated region, a 1053-bp ORF, and a 180-bp 3'-untranslated region. The ORF codes for a protein consisting of 350 amino acid residues and there existed one putative transmembrane domain. Figure 39 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 40 kDa that was almost identical with the molecular weight of 39,285 predicted from the ORF. In this case, the addition of a microsome led to the formation of a product of

100

43 kDa which is considered to have a sugar chain being attached. In addition, there exist in the amino acid sequence of this protein two sites at which N-glycosylation may occur (Asn-Asn-Ser at position 144 and Asn-Leu-Thr at position 328).

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA461346) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10591> (SEQ ID Nos. 100, 110, and 120)

Determination of the whole base sequence of the cDNA insert of clone HP10591 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 232-bp 5'-untranslated region, a 324-bp ORF, and a 844-bp 3'-untranslated region. The ORF codes for a protein consisting of 107 amino acid residues and there existed one putative transmembrane domain. Figure 40 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 11,328 predicted from the ORF.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H09424) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

of the present invention.

<HP01462> (SEQ ID Nos. 121, 131, and 141)

Determination of the whole base sequence of the cDNA  
 Insert of clone HP01462 obtained from cDNA library of human  
 fibrosarcoma cell line HT-1080 revealed the structure  
 consisting of a 121-bp 5'-untranslated region, a 1452-bp ORF,  
 and a 477-bp 3'-untranslated region. The ORF codes for a  
 protein consisting of 483 amino acid residues and there  
 existed a putative secretory signal at the N-terminus.  
 Figure 41 depicts the hydrophobicity/hydrophilicity profile,  
 obtained by the Kyte-Doolittle method, of the present  
 protein. In vitro translation resulted in formation of a  
 translation product of 72 kDa that was larger than the  
 molecular weight of 55,838 predicted from the ORF.  
 Application of the (-3,-1) rule, a method for predicting the  
 cleavage site of the secretory signal sequence, allows to  
 expect that the mature protein starts from lysine at  
 position 21.

The search of the protein data base using the amino  
 acid sequence of the present protein revealed that the  
 protein was similar to the *Caenorhabditis elegans*  
 hypothetical protein ZK1058.4 (EMBL Accession No. Z35604).  
 Table 27 shows the comparison between amino acid sequences  
 of the human protein of the present invention (HP) and the *C.*  
*elegans* hypothetical protein ZK1058.4 (CE). Therein, the  
 marks of -, \*, and . represent a gap, an amino acid residue  
 identical with that of the protein of the present invention,  
 and an amino acid residue similar to that of the protein of  
 the present invention, respectively. The both proteins  
 shared a homology of 35.6% in the entire region.

Table 27

	HP	MKAHFTFCVLLVFGSVSEAKFDDEEDIVEYDDNDFAEFEDVMEDSVTSQRVIIT	
			* *
5	CE	HP EDDE-DETVVELEGQENQEGDFEDADTQEGTSEFPYDDEEPEGYEDRP-----D	MKIWIWIFLFFIGFAIST
		* * * * * . . . . . * * * * * . . . . . * * * * *	
	CE	DDNEFAEFEDFVGSSATQAEIQREGEPVVKQKODFEEDFCGVVEEPEEAEKKEAD	
	HP	TSSSKNKDPITIVDPAPHLQNSWESYYLEILMWTLGLLAYIMNYIIGKNKNSRLAQAFNT	
10		* * * * * . . . . . * * * * * . . . . . * * * * *	
	CE	SDAAPAPLKPADVPFAHFRSNWASYQVEGIVLILIIYINWYILGKTTWASTAQIFDM	
	HP	HRELLESNFTLVGGDGTNKEATSTGKLNQNEHIYNLWCSGRVCCGMLIQLFLKRDLL	
		* * * * * . . . . . * * * * * . . . . . * * * * *	
	CE	CRPTLEQFVVGDDGTTDLDKHIPSLKHDTSTFSAWCTGRVNVNSLFLQNMVRQDV	
15	HP	LNVLARMRPVSDQVQIKVTNN-DEDMTVYFVAGTRKALVRLQKEMQDLSEFCSDKPKS	
		. . . * * * * * . . . . . * * * * * . . . . . * * * * *	
	CE	VSRIHEMTTPSGDKMTIKASLETNTDPLIFAVGKKIASKYFKEMLDLNSFASERKQA	
	HP	GARYGLPDSLAILSEMGVTDGMDTRMWHFLTHYADKIESVHFSQFSGPKINQEGQP	
		* * * * * . . . . . * * * * * . . . . . * * * * *	
20	CE	AQQNLPAWQVYADQNEVVFSLDPGVVSLKKKHDAIEFIIHSQFTGFKPAEGESYT	
	HP	LKLPDTKRTLLFTFNVPGSGNTYPKDMEALLPLANNMVIYSIDKAKFRANREGKQADKN	
		* * * * * . . . . . * * * * * . . . . . * * * * *	
	CE	-RLPEAQRYMFWSLNQLVIG----QDEESVMEILNLVYLIDKARKHKLSKDAKVAERR	
	HP	RARVEENFLKLTHTVORQEAQSRREKKRAEKERIMNEEDPEKQRLAEAAAREQKLE	
25		* * * * * . . . . . * * * * * . . . . . * * * * *	
	CE	RKEFEDAFLKQTHQFROEAQAARREKTRERKQKLMDSDPERKRLAEKELKREAKA--	
	HP	KKQMKKQLKVKEM	
		* * * * *	
	CE	-KSPMKKQLKVK	
30			

Furthermore, the search of the GenBank using the base  
 sequences of the present cDNA has revealed the registration  
 of sequences that shared a homology of 90% or more (for

example, Accession No. AA307793) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02485> (SEQ ID Nos. 122, 132, and 142)

Determination of the whole base sequence of the cDNA insert of clone HP02485 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 69-bp 5'-untranslated region, a 1005-bp ORF, and a 1672-bp 3'-untranslated region. The ORF codes for a protein consisting of 334 amino acid residues and there existed one putative transmembrane domain. Figure 42 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 36 kDa that was almost identical with the molecular weight of 38,171 predicted from the ORF. When expressed in COS7 cells, an expression product of about 23 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the Caenorhabditis elegans hypothetical protein W01A11.2 (Genbank Accession No. U64852). Table 28 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the C. elegans hypothetical protein W01A11.2 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 45.5% in the entire region.

Table 28

HP	MVEAPLPMPERRLQTLAVLQVPSFLAETCT-V
CE	.....*
HP	MRRLSSISGKNTLPDKICSSVSRLAPLVPKRRLETAVGFIEMVILINDLW
CE	.....*
HP	GPIALLFTFRFWLLTVLYAMWYLDRDKRQGGRIIQAIRCTTIKRYKDYPPISLVKTAE
CE	.....*
HP	PFHVLFTFMWFLVPLVAVWFYDDTEPKASRRMNAARVANKYASYPPLNLITAD
CE	.....*
HP	LDPSRNYIAGFBHGVLAAGAAANLCTESTGSSIFPGIRPHIMLTLMPRAPPPDYIM
CE	.....*
HP	LPADRNYIIGSHGMSVSGFTAMSTNATGFEKPGIKSHIMTLNGQYFPFRREGI
CE	.....*
HP	SAGLVTSKESAAHILNRKGGNLIIGVGNQALDARPGSFYLLRNKRGVRLATF
CE	.....*
HP	MGIEVSKESLEVTTCGKGRACAIVTIGASBALAHPPKNTLTILNRGCKYALNF
CE	.....*
HP	GAPLVPIFSFGENDLPDQIPNSGSLNRYIQNRLOKIMGISLPLFHRGVF-QYSFELIP
CE	.....*
HP	GADLVPMYNGENDLYEQYENPKGSRINREVQEKIKDFGLCPPLNRGSLFNQYLIGLP
CE	.....*
HP	YRRPITTVGKPIEVGKTLHPSEEVNQLHORVKEICNLFEAKLKNFIPADQHLEFC
CE	.....*
HP	FRKPVTVVNGRPIRVLTQDEPVEQIDELHAKYCDALYNLPFEYKHLHSIPDTHLIFQ
CE	.....*

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D25664) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP02798> (SEQ ID Nos. 123, 133, and 143)

Determination of the whole base sequence of the cDNA

insert of clone HP02798 obtained from cDNA library of human fibrosarcoma cell line HT-1080 revealed the structure consisting of a 31-bp 5'-untranslated region, a 804-bp ORF, and a 301-bp 3'-untranslated region. The ORF codes for a protein consisting of 267 amino acid residues and there existed four putative transmembrane domains. Figure 43 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 29 kDa that was almost identical with the molecular weight of 30,778 predicted from the ORF. When expressed in COS7 cells, an expression product of about 26 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human DHHC-containing cysteine-rich protein (GenBank Accession No. U90653). Table 29 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human DHHC-containing cysteine-rich protein (DH). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 35.0% in the intermediate region of 100 amino acid residues. The positions of seven cysteines were conserved between the two proteins. The protein of the present invention also had the DHHC (Asp-His-His-Cys) sequence.

Table 29

```

HP      MAPWALLSPGVLVRTGHTVLTWGI
5      DH MYRMNICNPSNKTAPESVVTAPQPSPELQGSRNRGWSWPHPPLQIVAMLLYL
HP      TLVTLFHDTELQWEEQELLEPLTFLLLVLGSLLLYAVSLADPGYVNVQPQ-QEELK
      * * * * *
10     DH FFAVICGILVPLPHHWVPAGYACMGALPAGHVLVHLTAVSIDPADDNVRDKSVAGPLP
HP      EEQANTVPAIPALRCRYCIVLQPLBARHCHRECRVRRYDHHCPWMENCVCGERNHPLFV
      * * * * *
15     DH IFNRSOAHVIEDLHCNLNVDSARKSKHCSACNKCVCGEDHCKWLNCCVGRNYRFL
HP      VYIALQVLVLMGLYLAWSGLRFFQPNGLMRLRSGLLFATFLLLSLFSLVASLLLVSHLY
      * * * * *
DH      HSVASALLGVLLLVGGHICLRGVLCOPHASAHQPTL

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. D79050) In ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

25 : <HP10041> (SEO ID Nos. 124, 134, and 144)

Determination of the whole base sequence of the cDNA insert of clone HP10041 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 12-bp 5'-untranslated region, a 321-bp ORF, and a 286-bp 3'-untranslated region. The ORF codes for a protein consisting of 106 amino acid residues and there existed one putative transmembrane domain. Figure 44 depicts



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the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 12 kDa that was almost identical with the molecular weight of 12,060 predicted from the ORF. When expressed in COS7 cells, an expression product of about 13 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Caenorhabditis elegans* hypothetical protein K10B2.4 (GenBank Accession No. U28730). Table 30 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *C. elegans* hypothetical protein K10B2.4 (CE). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The both proteins shared a homology of 62.1% in the entire region.

Table 30

```

HP MSTNNNDPDRRRPKVLRYKP---PPSECDALDDPPDPYKMLGMIFSMCGMLKRWCA
      ***** ..... ** *.....*****
CE MOONGDPRTNRIVRYKPLDSTANQQAISEDPLEKYNNVLGMIFSMCGMLIRKNCES
HP WVAAYCSFISFANRSSEDTKQWMSFMLSISAVVMSYLLNQPPQMPMPM
      *****.....*****
CE WLAIVCSGISFANRTSDAKQIVSFMLSVSAVMSYLLNQPPPIIPWVTLLOS

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Furthermore, the search of the GenBank using the base

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sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H20098) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10246> (SEQ ID Nos. 125, 135, and 145)

Determination of the whole base sequence of the cDNA insert of clone HP10246 obtained from cDNA library of human epidermoid carcinoma cell line KB revealed the structure consisting of a 110-bp 5'-untranslated region, a 675-bp ORF, and a 79-bp 3'-untranslated region. The ORF codes for a protein consisting of 224 amino acid residues and there existed five putative transmembrane domains. Figure 45 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 23 kDa that was somewhat smaller than the molecular weight of 25,244 predicted from the ORF. When expressed in COS7 cells, an expression product of about 21 kDa was observed in the membrane fraction.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the human putative seven transmembrane domain protein (GenBank Accession No. Y18007). Table 31 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the human putative seven transmembrane domain protein (TM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that

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of the protein of the present invention, respectively. The both proteins shared a homology of 93.3% in the entire region.

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Table 31

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HP MTLFHFNCFPALAYFPYFITYKCSGLSEYNFKNVCQAGVTYLFVOLCKMFLATFFPTW
*****
TM MTLFHFNCFPALAYFPYFITYKCTDLSEYNFKNVCQAGVTYLFVOLCKMFLATFFPTW
HP EGGIYDFIGFMKASVDVADLIGLNLVMSRNAGKEIKIMVAALGWATAELINSRCIPLW
*****
TM EGGIYDFIGFMKASVDVADLIGLNLVMSRNAGKEIKIMVAALGWATAELINSRCIPLW
HP VGARGIEFDWKYIQMSIDSNISLVHYIVASQVWMITRYDLYHTFRPAVLLMFLSVYKA
*****
TM VGARGIEFDWKYIQMSIDSNISLGPYIVASQVWMITRYDLYHTFRPAVLLMFLSVYKA
HP FMVETFVHLCSLGSMAALLARAVVTGLLALSTALYVAVVNVHS
*****
TM FMVETFVHLCSLGSMAVLMAGVVVKGLLVIRNLAMYVAVVNVHS
```

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Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA453931) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

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<HP10392> (SEQ ID Nos. 126, 136, and 146)

30 Determination of the whole base sequence of the cDNA insert of clone HP10392 obtained from cDNA library of human osteosarcoma cell line U-2 OS revealed the structure

consisting of a 24-bp 5'-untranslated region, a 777-bp ORF, and a 726-bp 3'-untranslated region. The ORF codes for a protein consisting of 258 amino acid residues and there existed a putative secretory signal at the N-terminus. Figure 46 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 34 kDa that was somewhat larger than the molecular weight of 29,623 predicted from the ORF. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from leucine at position 49.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. H15999) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention. In addition, partial identity with the hypothetical protein KIAA0384 (Accession No. AB002382) was observed, although the hypothetical protein had a different ORF.

25 <HP10489> (SEQ ID Nos. 127, 137, and 147)

Determination of the whole base sequence of the cDNA insert of clone HP10489 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 137-bp 5'-untranslated region, a 333-bp ORF, and a 189-bp 3'-untranslated region. The ORF codes for a protein consisting of 110 amino acid residues and there existed two putative transmembrane domains. Figure 47 depicts the

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hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 19 kDa that was somewhat larger than the molecular weight of 12,010 predicted from the ORF.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AA262162) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10519> (SEQ ID Nos. 128, 138, and 148)

Determination of the whole base sequence of the cDNA insert of clone HP10519 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 67-bp 5'-untranslated region, a 276-bp ORF, and a 367-bp 3'-untranslated region. The ORF codes for a protein consisting of 91 amino acid residues and there existed one putative transmembrane domain. Figure 48 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of 10 kDa that was almost identical with the molecular weight of 10,275 predicted from the ORF.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. W16639) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein

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of the present invention.

<HP10531> (SEQ ID Nos. 129, 139, and 149)

Determination of the whole base sequence of the cDNA insert of clone HP10531 obtained from cDNA library of human osteosarcoma cell line Saos-2 revealed the structure consisting of a 55-bp 5'-untranslated region, a 1035-bp ORF, and a 1092-bp 3'-untranslated region. The ORF codes for a protein consisting of 344 amino acid residues and there existed five putative transmembrane domains. Figure 49 depicts the hydrophobicity/hydrophilicity profile, obtained by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight.

Furthermore, the search of the Genbank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. R50695) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

<HP10574> (SEQ ID Nos. 130, 140, and 150)

Determination of the whole base sequence of the cDNA insert of clone HP10574 obtained from cDNA library of human stomach cancer revealed the structure consisting of a 210-bp 5'-untranslated region, a 1287-bp ORF, and a 1276-bp 3'-untranslated region. The ORF codes for a protein consisting of 428 amino acid residues and there existed a putative secretory signal at the N-terminus and one putative transmembrane domain in the intermediate region. Figure 50 depicts the hydrophobicity/hydrophilicity profile, obtained

by the Kyte-Doolittle method, of the present protein. In vitro translation resulted in formation of a translation product of high molecular weight. Application of the (-3,-1) rule, a method for predicting the cleavage site of the secretory signal sequence, allows to expect that the mature protein starts from serine at position 36.

The search of the protein data base using the amino acid sequence of the present protein revealed that the protein was similar to the *Drosophila melanogaster* GOLIATH protein (SWISS-PROT Accession No. Q06003). Table 32 shows the comparison between amino acid sequences of the human protein of the present invention (HP) and the *D. melanogaster* GOLIATH protein (DM). Therein, the marks of -, \*, and . represent a gap, an amino acid residue identical with that of the protein of the present invention, and an amino acid residue similar to that of the protein of the present invention, respectively. The intermediate region of 169 amino acids of the protein of the present invention shared a homology of 41.4% with the N-terminal region of the *D. melanogaster* GOLIATH protein.

Furthermore, the search of the GenBank using the base sequences of the present cDNA has revealed the registration of sequences that shared a homology of 90% or more (for example, Accession No. AAL55685) in ESTs, but, since they are partial sequences, it can not be judged whether or not any of these sequences codes for the same protein as the protein of the present invention.

## INDUSTRIAL APPLICABILITY

Table 32

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5  HP MGPPPGAGVSCRGCGFSRLLAWCFLLALSPOARSGRGAEAUWTAYLNVSRVPHPTGVN
HP TWWEELSEGVYQODSPLEPNAGVLPDPDGCALNACPHNTFTVPTVWGSTVQVSWLALI
HP QRGCGCTFADKTHLAYERGASGAVIFNPPGTRNEZVPHSHPGAVDIYAIMIGNLKTKIL
    * * * * *
DM MQLKMQIKGKTRNIAAIVTYQNIQDLS
HP QSIQRGIQVWTVIEVGKK---HGPWVNHYSIFFVSUVEFFIITATVGYFFPYPSARLRUNA
    * * * * *
DM LTLDKGVNVTISIERRGVRTISSLARTSVLFVSIIS-FIV-DDILCWLFFYYIQFRYM
HP RAQRKQORQLADAKAKAIGRLQLRHLTKQGDKEIGFDGSDCAVCIELXKPNDLVRLTCNH
    * * * * *
DM QAKDQQRNLCSVTIKKAIKIMPTTKGFS-D-EKOLDSDCAICEAVKPTDTRIILPCKH
HP IFHKTCVDPELLEHRTCPMKCDILKALGIEVOVEDGSVSLQVPVSNESINSASSHEEDN
    * * * * *
DM EFHKNCIDPELLEHRTCPMKCLDVLFYGYVVGDOIYQTPSPQHTAFIASIEEVPVIUWA
HP RSETASSGYASVQGTDEPPELLEHVQSTNESLQLVNHANSVADVIPHVDNPTFEDETPT
    * * * * *
DM VPHGPOPLQLOASNNSFAPSHYFQSSRSPSSVQQOOLAPLTVQPHPOQAASERGRNS
HP NQETAVREIKS
DM APATMPEHATAGHOVTDV

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The present invention provides human proteins having hydrophobic domains, DNAs coding for these proteins, and expression vectors for these DNAs as well as eucaryotic cells expressing these DNAs. All of the proteins of the present invention are secreted or exist in the cell membrane, so that they are considered to be proteins controlling the proliferation and/or the differentiation of the cells. Accordingly, the proteins of the present invention can be employed as pharmaceuticals such as carcinostatic agents which act to control the proliferation and/or the differentiation of the cells, or as antigens for preparing antibodies against these proteins. The DNAs of the present invention can be utilized as probes for the genetic diagnosis and gene sources for the gene therapy. Furthermore, the DNAs can be utilized for large-scale expression of these proteins. Cells into which these genes are introduced to express these proteins, can be utilized for detection of the corresponding receptors and ligands, screening of novel low-molecular pharmaceuticals, and so on.

The present invention also provides genes corresponding to the polynucleotide sequences disclosed herein. "Corresponding genes" are the regions of the genome that are transcribed to produce the mRNAs from which cDNA polynucleotide sequences are derived and may include contiguous regions of the genome necessary for the regulated expression of such genes. Corresponding genes may therefore include but are not limited to coding sequences, 5' and 3' untranslated regions, alternatively spliced exons, introns, promoters, enhancers, and silencer or suppressor elements. The corresponding genes can be isolated in accordance with known methods using the sequence information disclosed herein. Such methods include the preparation of probes or

primers from the disclosed sequence information for identification and/or amplification of genes in appropriate genomic libraries or other sources of genomic materials. An "isolated gene" is a gene that has been separated from the adjacent coding sequences, if any, present in the genome of the organism from which the gene was isolated.

Organisms that have enhanced, reduced, or modified expression of the gene(s) corresponding to the polynucleotide sequences disclosed herein are provided. The desired change in gene expression can be achieved through the use of antisense polynucleotides or ribozymes that bind and/or cleave the mRNA transcribed from the gene (Albert and Morris, 1994, *Trends Pharmacol. Sci.* 15(7): 250-254; Lavarosky et al., 1997, *Biochem. Mol. Med.* 62(1): 11-22; and Hampel, 1998, *Prog. Nucleic Acid Res. Mol. Biol.* 58: 1-39; all of which are incorporated by reference herein). Transgenic animals that have multiple copies of the gene(s) corresponding to the polynucleotide sequences disclosed herein, preferably produced by transformation of cells with genetic constructs that are stably maintained within the transformed cells and their progeny, are provided. Transgenic animals that have modified genetic control regions that increase or reduce gene expression levels, or that change temporal or spatial patterns of gene expression, are also provided (see European Patent No. 0 649 464 B1, incorporated by reference herein). In addition, organisms are provided in which the gene(s) corresponding to the polynucleotide sequences disclosed herein have been partially or completely inactivated, through insertion of extraneous sequences into the corresponding gene(s) or through deletion of all or part of the corresponding gene(s). Partial or complete gene inactivation can be accomplished

through insertion, preferably followed by imprecise excision, of transposable elements (Plasterk, 1992, Bioessays 14(9): 629-633; Zwaal et al., 1993, Proc. Natl. Acad. Sci. USA 90(16): 7431-7435; Clark et al., 1994, Proc. Natl. Acad. Sci. USA 91(2): 719-722; all of which are incorporated by reference herein), or through homologous recombination, preferably detected by positive/negative genetic selection strategies (Mansour et al., 1988, Nature 336: 348-352; U.S. Patent Nos. 5,464,764; 5,487,992; 5,627,059; 5,631,153; 5,614, 396; 5,616,491; and 5,679,523; all of which are incorporated by reference herein). These organisms with altered gene expression are preferably eukaryotes and more preferably are mammals. Such organisms are useful for the development of non-human models for the study of disorders involving the corresponding gene(s), and for the development of assay systems for the identification of molecules that interact with the protein product(s) of the corresponding gene(s). Where the protein of the present invention is membrane-bound (e.g., is a receptor), the present invention also provides for soluble forms of such protein. In such forms part or all of the intracellular and transmembrane domains of the protein are deleted such that the protein is fully secreted from the cell in which it is expressed. The intracellular and transmembrane domains of proteins of the invention can be identified in accordance with known techniques for determination of such domains from sequence information.

Proteins and protein fragments of the present invention include proteins with amino acid sequence lengths that are at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of a disclosed protein and have at least 60% sequence identity (more

preferably, at least 75% identity; most preferably at least 90% or 95% identity) with that disclosed protein, where sequence identity is determined by comparing the amino acid sequences of the proteins when aligned so as to maximize overlap and identity while minimizing sequence gaps. Also included in the present invention are proteins and protein fragments that contain a segment preferably comprising 8 or more (more preferably 20 or more, most preferably 30 or more) contiguous amino acids that shares at least 75% sequence identity (more preferably, at least 85% identity; most preferably at least 95% identity) with any such segment of any of the disclosed proteins.

Species homologs of the disclosed polynucleotides and proteins are also provided by the present invention. As used herein, a "species homologue" is a protein or polynucleotide with a different species of origin from that of a given protein or polynucleotide, but with significant sequence similarity to the given protein or polynucleotide, as determined by those of skill in the art. Species homologs may be isolated and identified by making suitable probes or primers from the sequences provided herein and screening a suitable nucleic acid source from the desired species.

The invention also encompasses allelic variants of the disclosed polynucleotides or proteins; that is, naturally-occurring alternative forms of the isolated polynucleotide which also encode proteins which are identical, homologous, or related to that encoded by the polynucleotides.

The invention also includes polynucleotides with sequences complementary to those of the polynucleotides disclosed herein.

The present invention also includes polynucleotides

capable of hybridizing under reduced stringency conditions, more preferably stringent conditions, and most preferably highly stringent conditions, to polynucleotides described herein. Examples of stringency conditions are shown in the table 33 below: highly stringent conditions are those that are at least as stringent as, for example, conditions A-F; stringent conditions are at least as stringent as, for example, conditions G-L; and reduced stringency conditions are at least as stringent as, for example, conditions M-R.

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Table 33

Stringency Condition	Polynucleotide Hybrid	Hybrid Length (bp) <sup>f</sup>	Hybridization Temperature and Buffer <sup>g</sup>	Wash Temperature and Buffer <sup>h</sup>
A	DNA : DNA	≥50	65°C; 1×SSC -or- 42°C; 1×SSC, 50% formamide	65°C; 0.3×SSC
B	DNA : DNA	<50	T <sub>h</sub> <sup>+</sup> ; 1×SSC	T <sub>h</sub> <sup>+</sup> ; 1×SSC
C	DNA : RNA	≥50	67°C; 1×SSC -or- 45°C; 1×SSC, 50% formamide	67°C; 0.3×SSC
D	DNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 1×SSC	T <sub>h</sub> <sup>+</sup> ; 1×SSC
E	RNA : RNA	≥50	70°C; 1×SSC -or- 60°C; 1×SSC, 50% formamide	70°C; 0.3×SSC
F	RNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 1×SSC	T <sub>h</sub> <sup>+</sup> ; 1×SSC
G	DNA : DNA	≥50	65°C; 4×SSC -or- 42°C; 4×SSC, 50% formamide	65°C; 1×SSC
H	DNA : DNA	<50	T <sub>h</sub> <sup>+</sup> ; 4×SSC	T <sub>h</sub> <sup>+</sup> ; 4×SSC
I	DNA : RNA	≥50	67°C; 4×SSC -or- 45°C; 4×SSC, 50% formamide	67°C; 1×SSC
J	DNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 4×SSC	T <sub>h</sub> <sup>+</sup> ; 4×SSC
K	RNA : RNA	≥50	70°C; 4×SSC -or- 60°C; 4×SSC, 50% formamide	67°C; 1×SSC
L	RNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 2×SSC	T <sub>h</sub> <sup>+</sup> ; 2×SSC
M	DNA : DNA	≥50	60°C; 4×SSC -or- 40°C; 6×SSC, 50% formamide	60°C; 2×SSC
N	DNA : DNA	<50	T <sub>h</sub> <sup>+</sup> ; 6×SSC	T <sub>h</sub> <sup>+</sup> ; 6×SSC
O	DNA : RNA	≥50	55°C; 4×SSC -or- 42°C; 6×SSC, 50% formamide	55°C; 2×SSC
P	DNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 6×SSC	T <sub>h</sub> <sup>+</sup> ; 6×SSC
Q	RNA : RNA	≥50	60°C; 4×SSC -or- 45°C; 6×SSC, 50% formamide	60°C; 2×SSC
R	RNA : RNA	<50	T <sub>h</sub> <sup>+</sup> ; 4×SSC	T <sub>h</sub> <sup>+</sup> ; 4×SSC

<sup>f</sup>: The hybrid length is that anticipated for the hybridized region(s) of the hybridizing polynucleotides. When hybridizing a polynucleotide to a target polynucleotide of unknown sequence, the hybrid length is assumed to be that of the hybridizing polynucleotide. When polynucleotides of known sequence are hybridized, the hybrid length can be determined by aligning the sequences of the polynucleotides and identifying the region or regions of optimal sequence complementarity.

<sup>g</sup>: SSPE (1×SSPE is 0.15M NaCl, 10mM NaH<sub>2</sub>PO<sub>4</sub>, and 1.25mM EDTA, pH7.4) can be substituted for SSC (1×SSC is 0.15M NaCl and 15mM sodium citrate) in the hybridization and wash buffers; washes are performed for 15 minutes after hybridization is complete.

<sup>h</sup>: T<sub>h</sub> : T<sub>h</sub> : The hybridization temperature for hybrids anticipated to be less than

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50 base pairs in length should be 5-10°C less than the melting temperature ( $T_m$ ) of the hybrid, where  $T_m$  is determined according to the following equations. For hybrids less than 18 base pairs in length,  $T_m(°C) = 2(\# \text{ of A + T bases}) + 4(\# \text{ of G + C bases})$ . For hybrids between 18 and 49 base pairs in length,  $T_m(°C) = 81.5 + 16.6(\log_{10}[\text{Na}^+]) + 0.41(\% \text{ G+C}) - (600/N)$ , where N is the number of bases in the hybrid, and  $[\text{Na}^+]$  is the concentration of sodium ions in the hybridization buffer ( $[\text{Na}^+]$  for 1×SSC=0.165M).

Additional examples of stringency conditions for polynucleotide hybridization are provided in Sambrook, J., E.F. Fritsch, and T. Maniatis, 1989, Molecular Cloning: A Laboratory Manual, Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY, chapters 9 and 11, and Current Protocols in Molecular Biology, 1995, F.M. Ausubel et al., eds., John Wiley & Sons, Inc., sections 2.10 and 6.3-6.4, incorporated herein by reference.

Preferably, each such hybridizing polynucleotide has a length that is at least 25% (more preferably at least 50%, and most preferably at least 75%) of the length of the polynucleotide of the present invention to which it hybridizes, and has at least 60% sequence identity (more preferably, at least 75% identity; most preferably at least 90% or 95% identity) with the polynucleotide of the present invention to which it hybridizes, where sequence identity is determined by comparing the sequences of the hybridizing polynucleotides when aligned so as to maximize overlap and identity while minimizing sequence gaps.

# CLAIMS

1. A protein comprising any one of an amino acid sequence selected from the group consisting of SEQ ID Nos. 1 to 10, 31 to 40, 61 to 70, 91 to 100, and 121 to 130.
2. An isolated DNA coding for the protein according to Claim 1.
3. An isolated cDNA comprising any one of a base sequence selected from the group consisting of SEQ ID Nos. 11 to 20, 41 to 50, 71 to 80, 101 to 110, and 131 to 140.
4. The cDNA according to Claim 3 consisting of any one of a base sequence selected from the group consisting of SEQ ID Nos. 21 to 30, 51 to 60, 81 to 90, 111 to 120, and 141 to 150.
5. An expression vector that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 by in vitro translation or in eucaryotic cells.
6. A transformed eucaryotic cell that is capable of expressing the DNA according to any one of Claim 2 to Claim 4 and of producing the protein according to Claim 1:



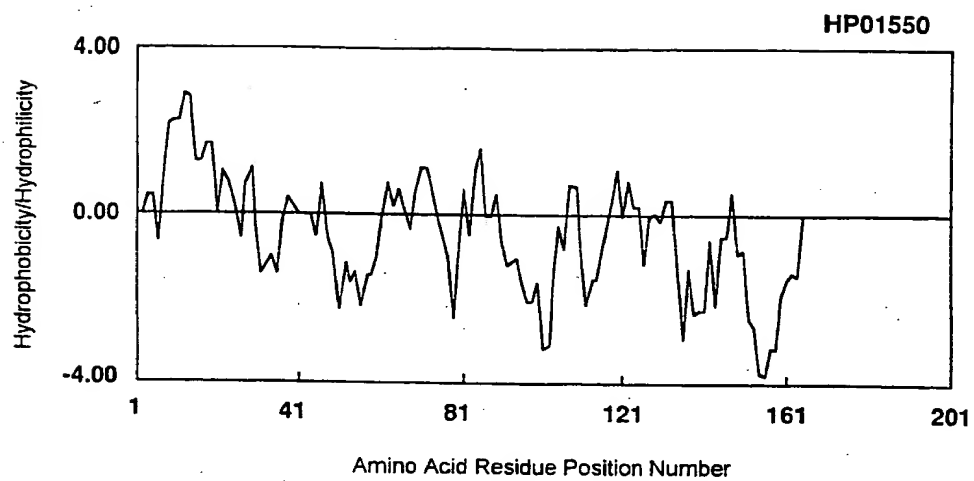


Fig. 1

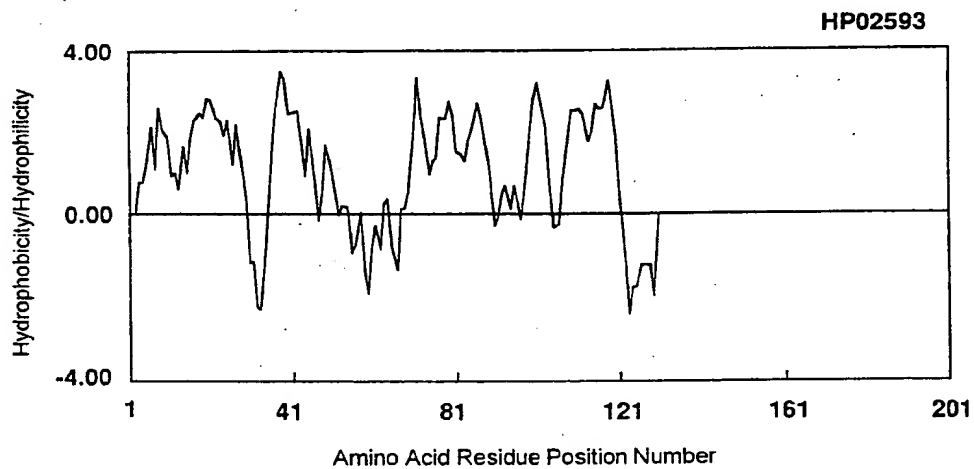


Fig. 2

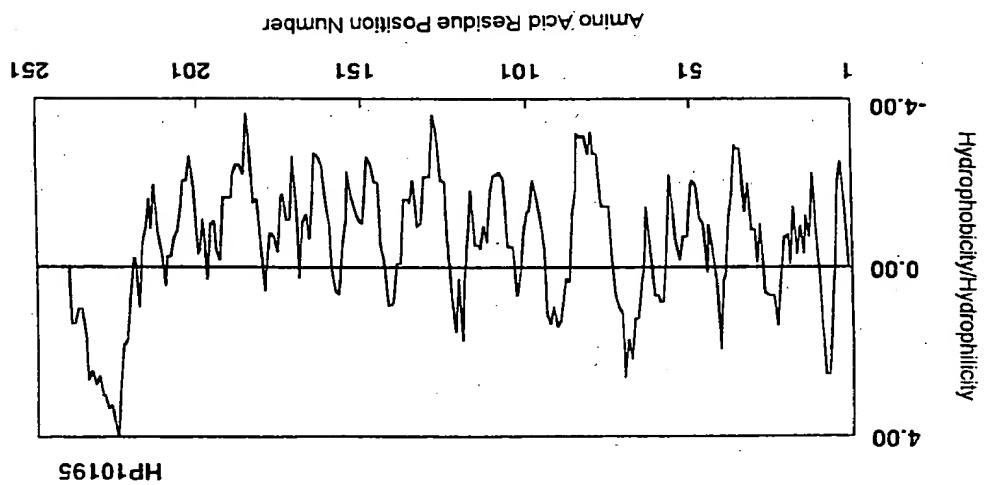


Fig. 3

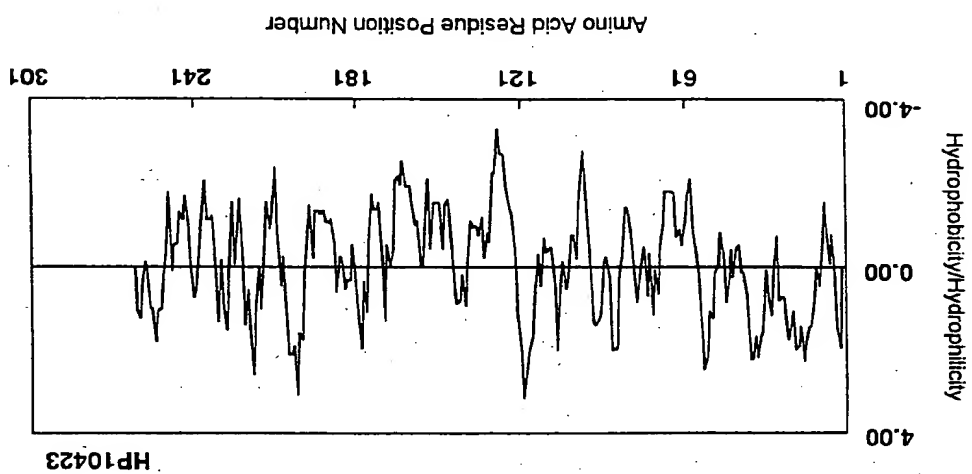


Fig. 4

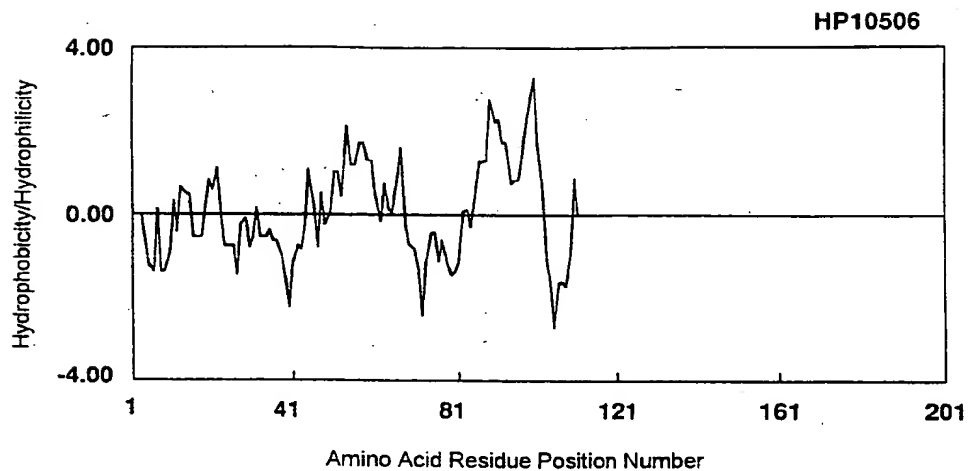


Fig. 5

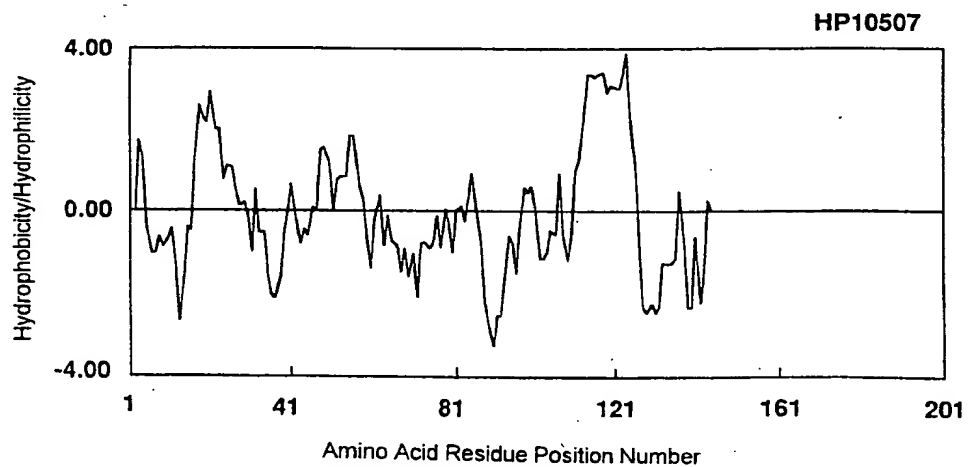


Fig. 6

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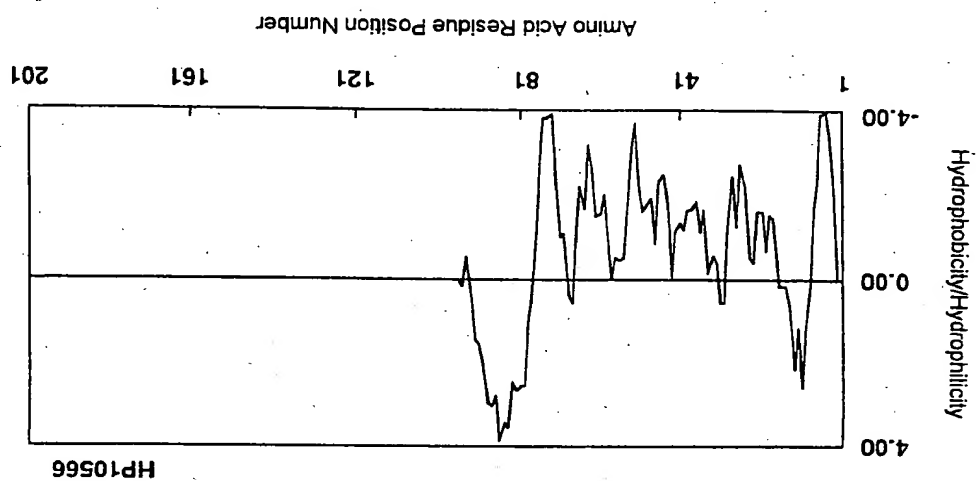


Fig. 8

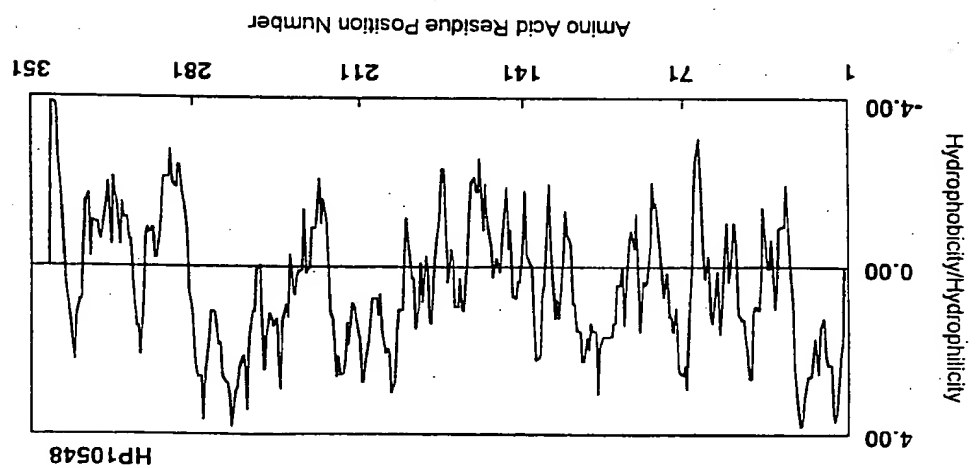


Fig. 7

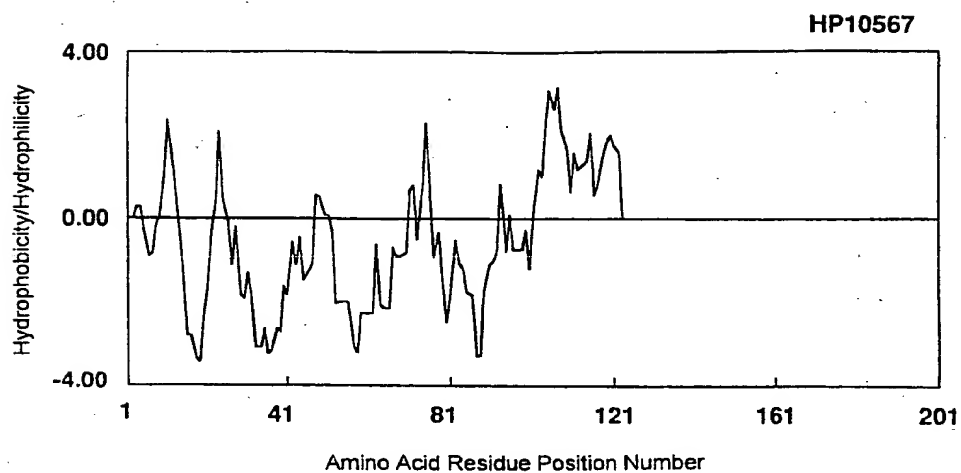


Fig. 9

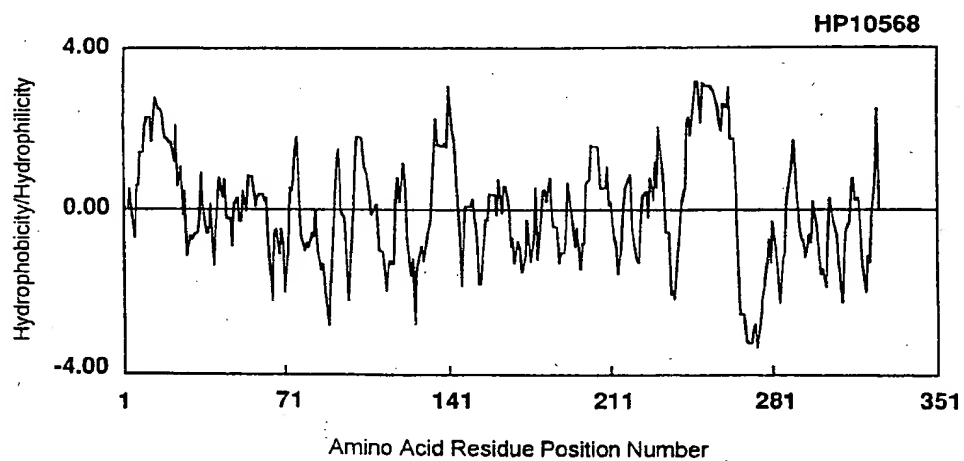


Fig. 10

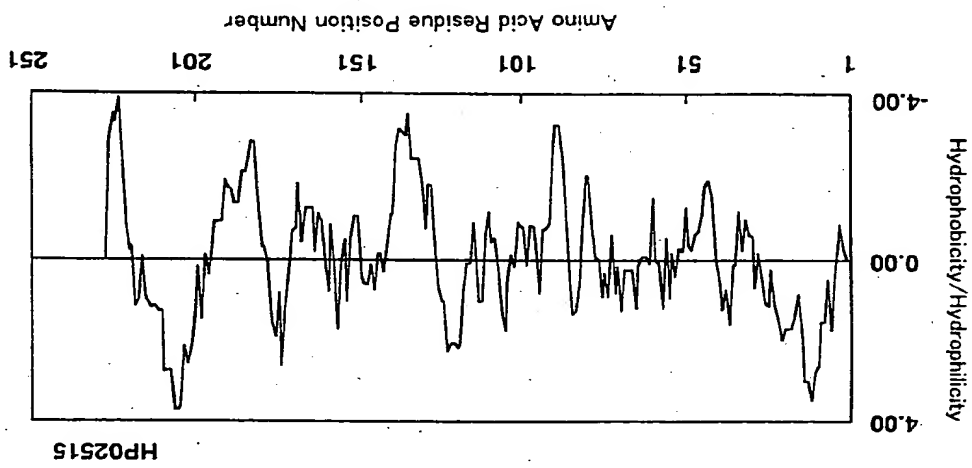


Fig. 12

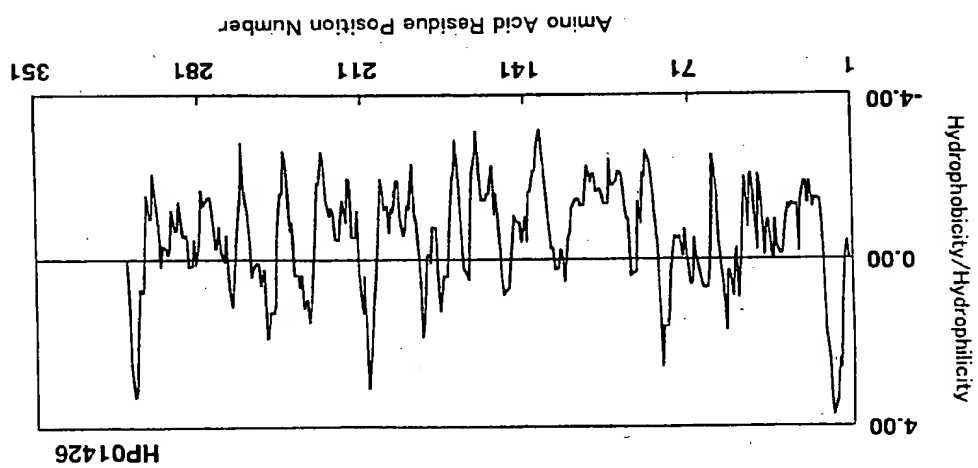


Fig. 11

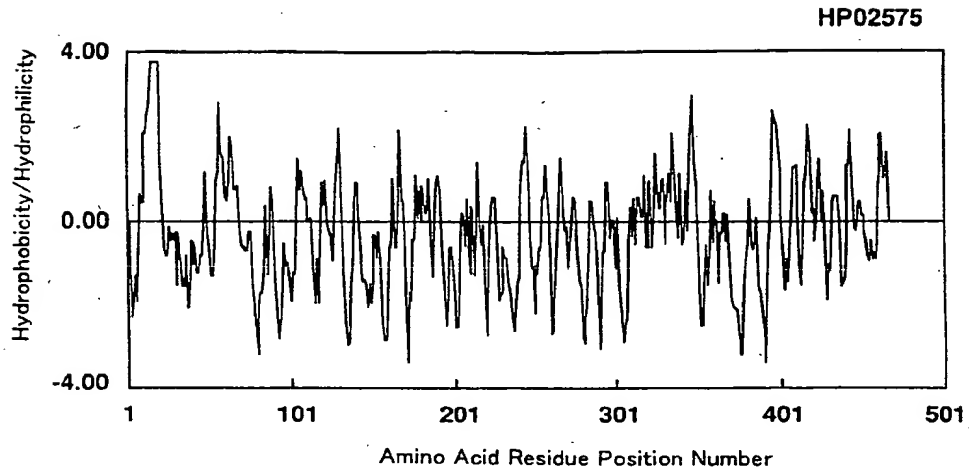


Fig. 13

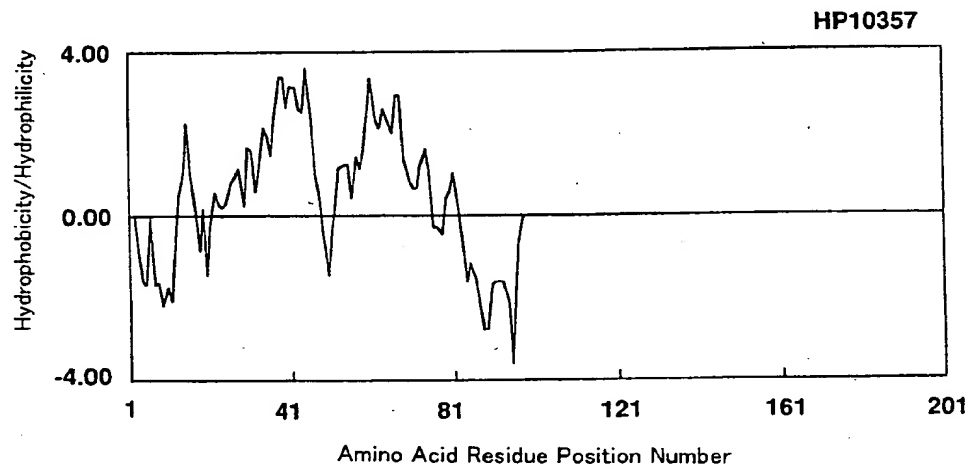


Fig. 14

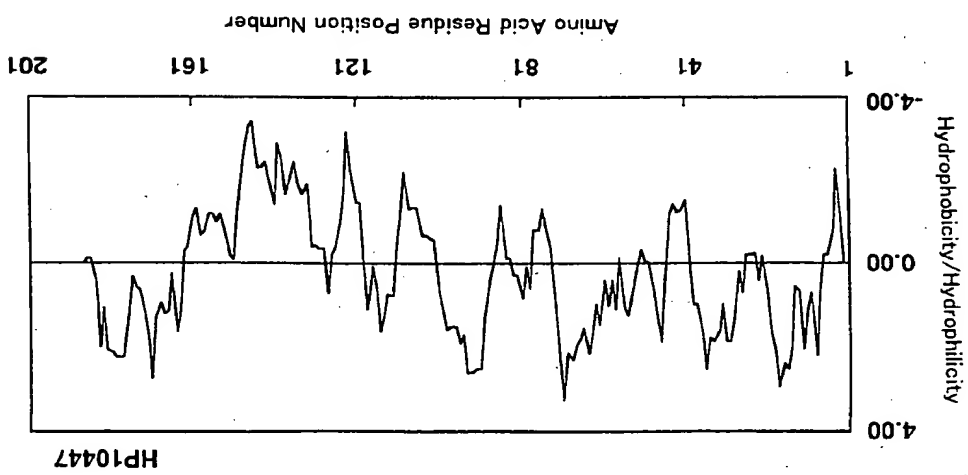


Fig. 15

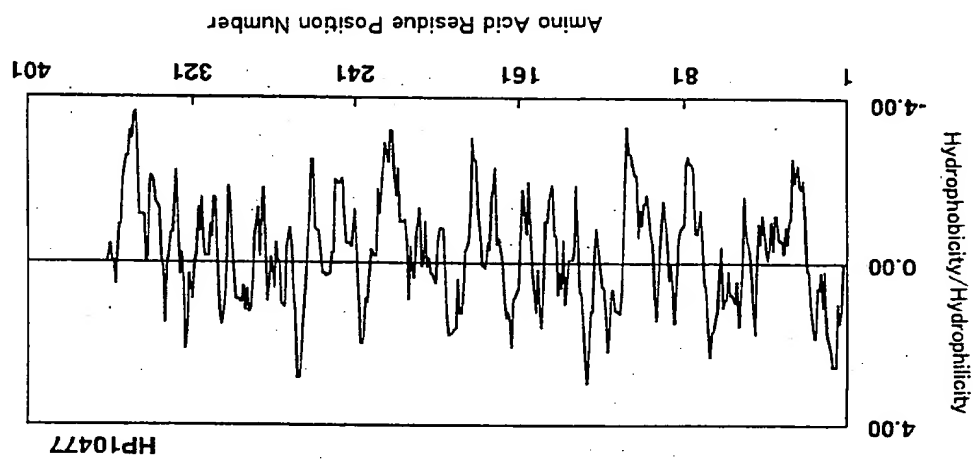


Fig. 16



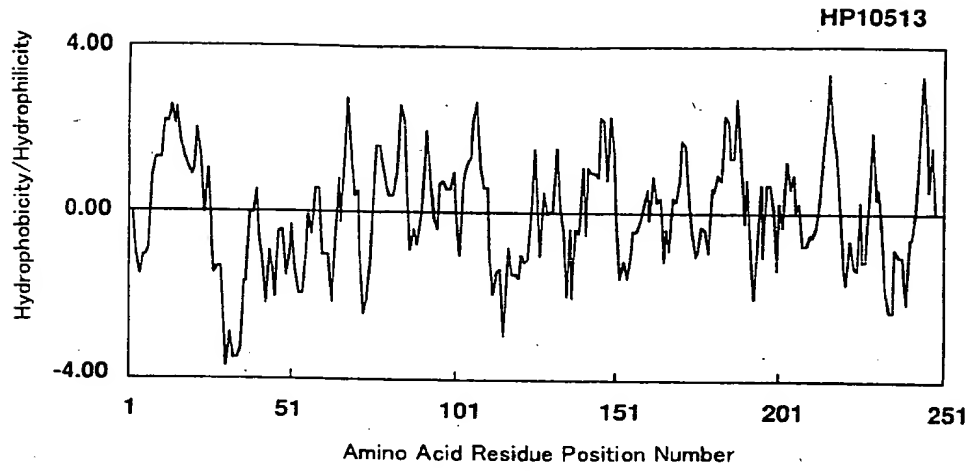


Fig.17

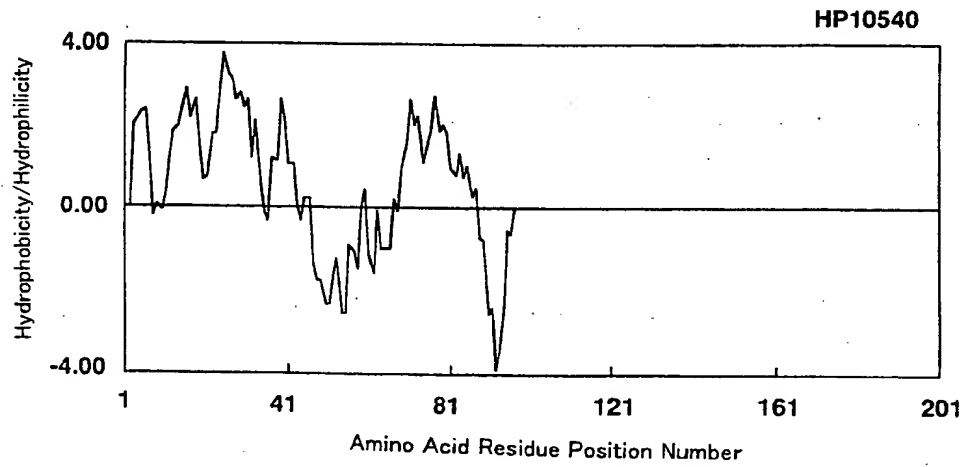


Fig. 18

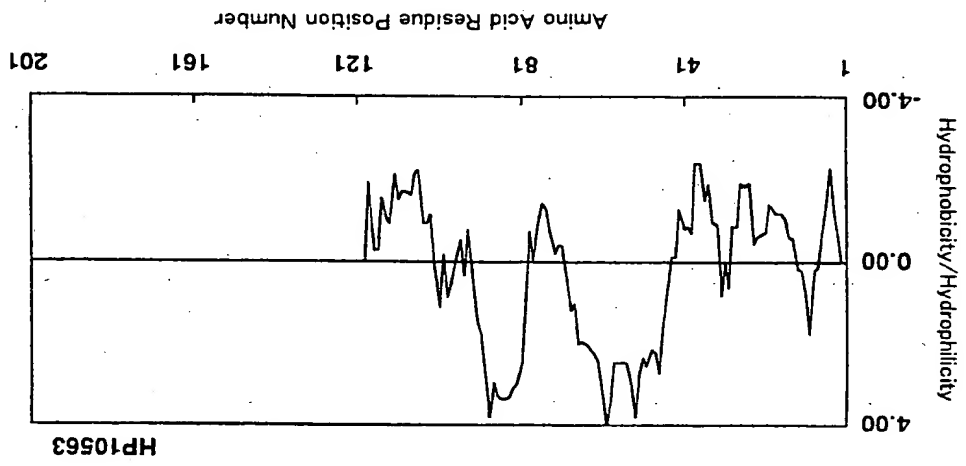


Fig. 20

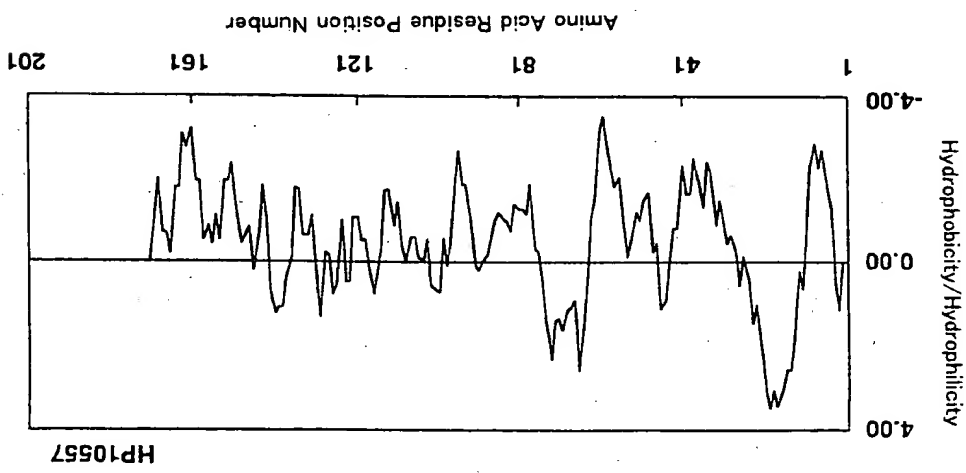


Fig. 19

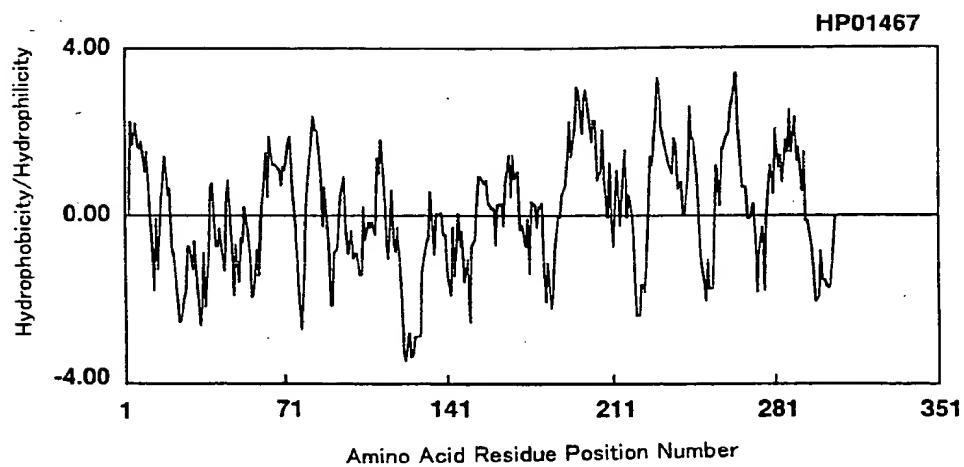


Fig. 21

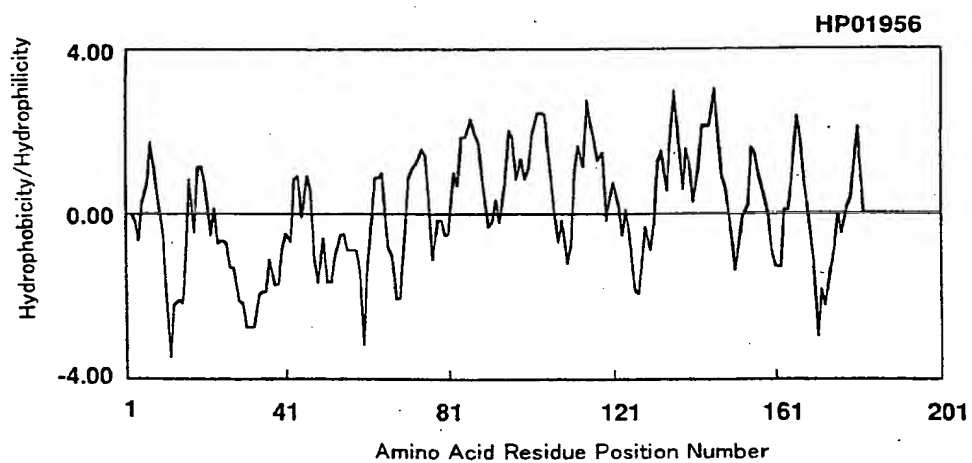


Fig.22

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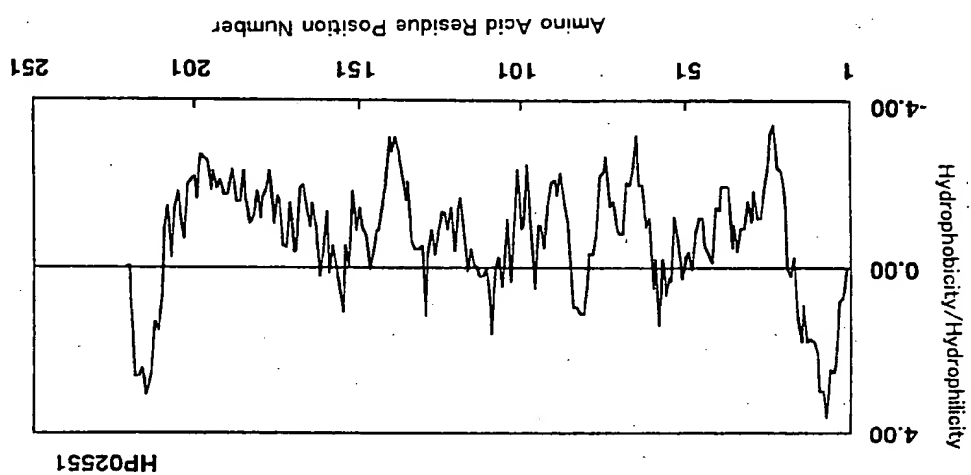


Fig. 24

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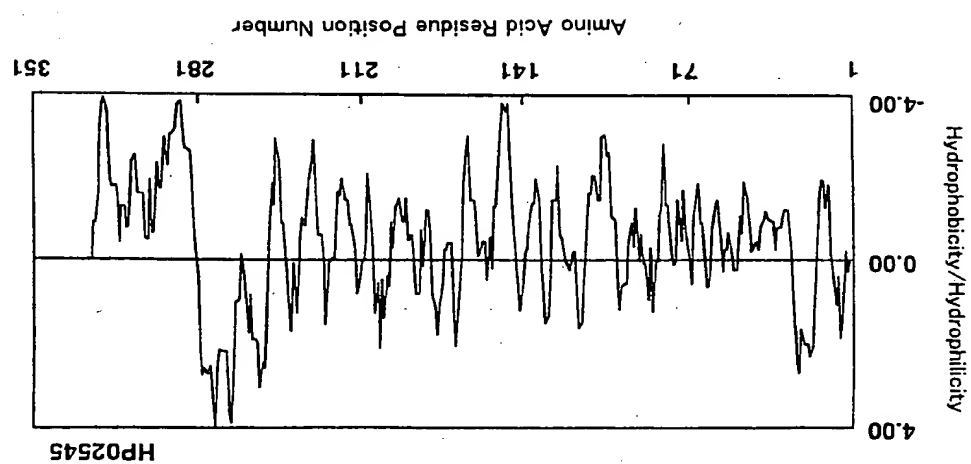


Fig. 23

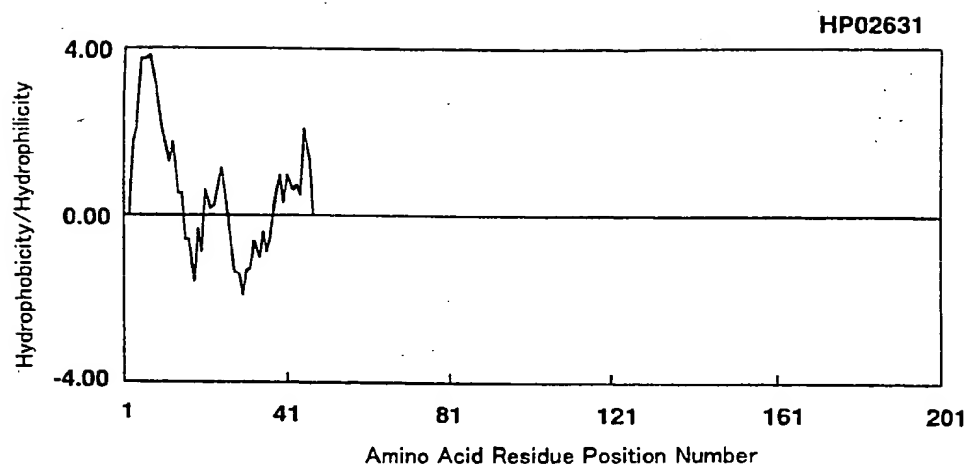


Fig. 25

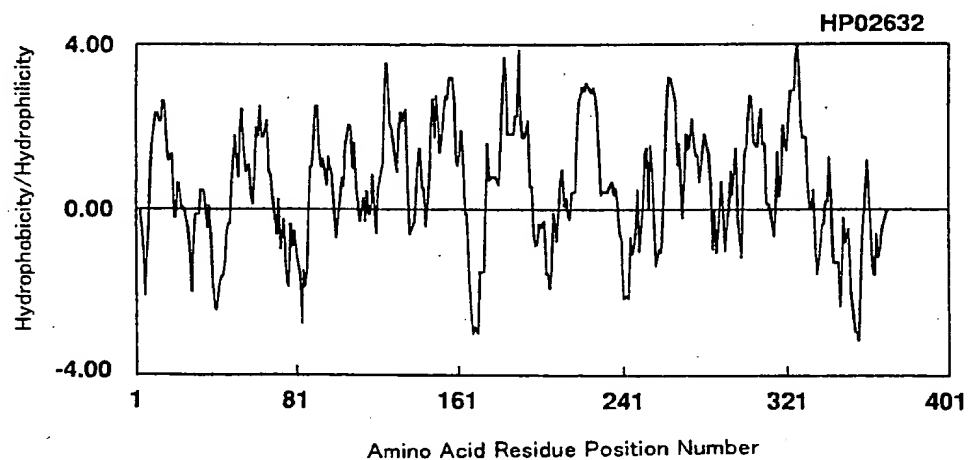


Fig. 26

Fig. 28

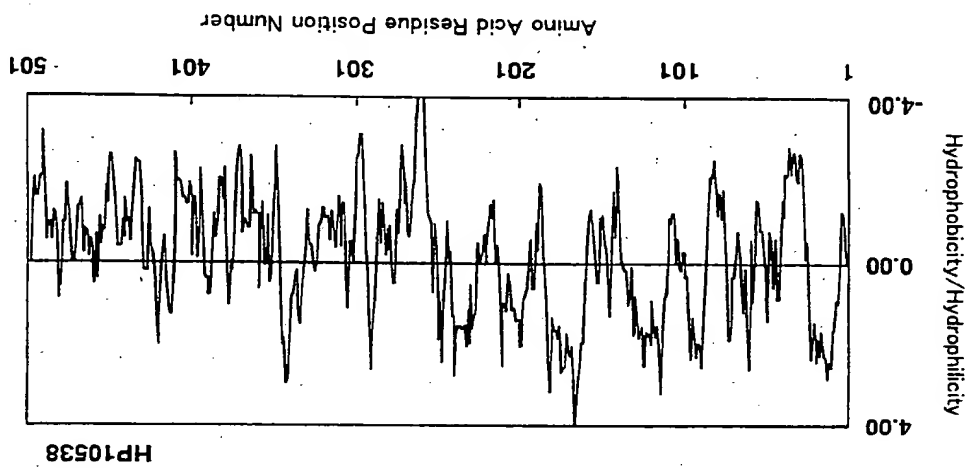
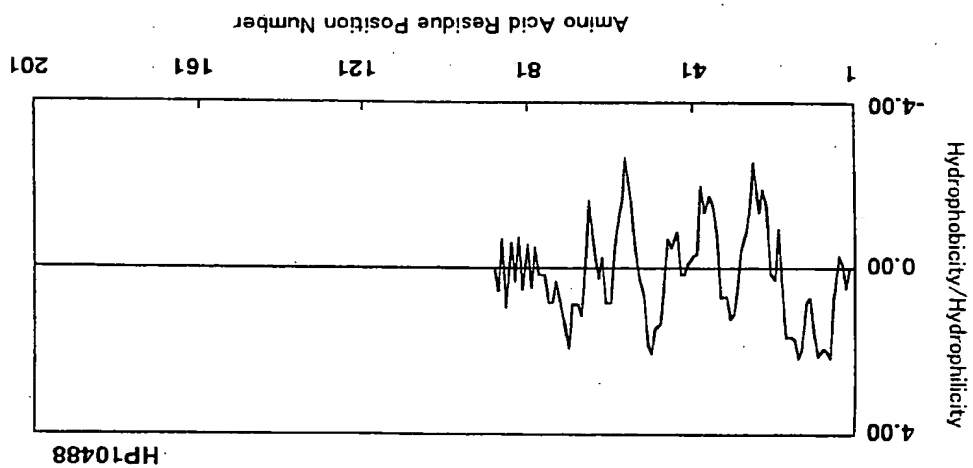


Fig. 27



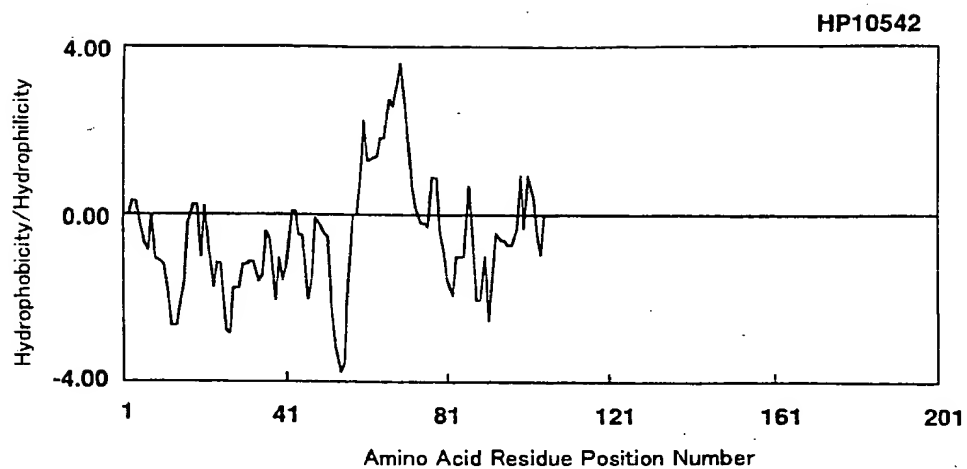


Fig. 29

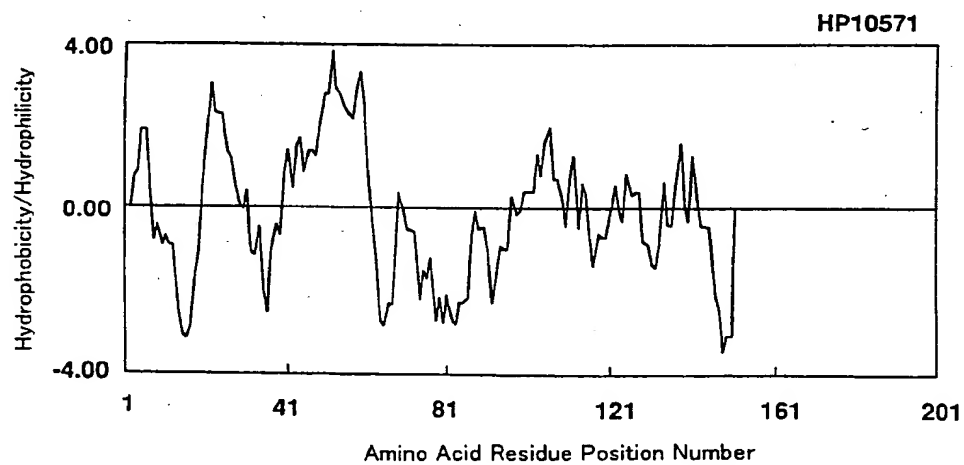


Fig. 30

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Fig. 32

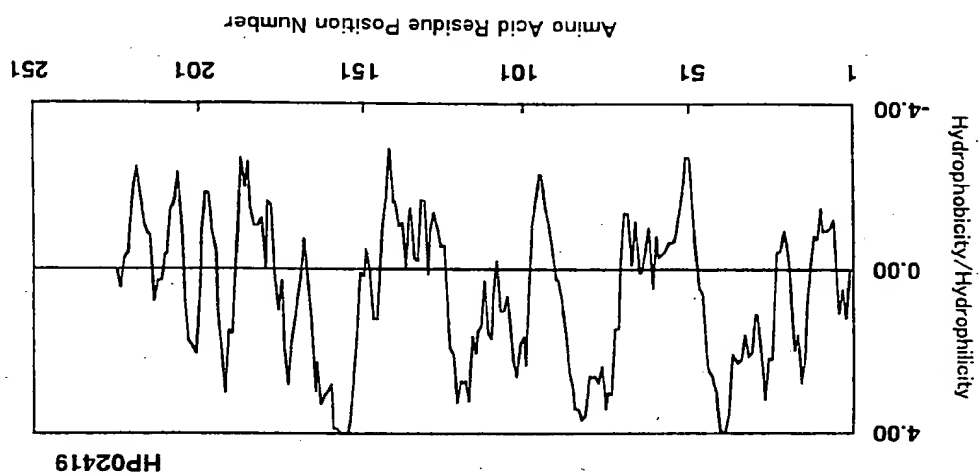
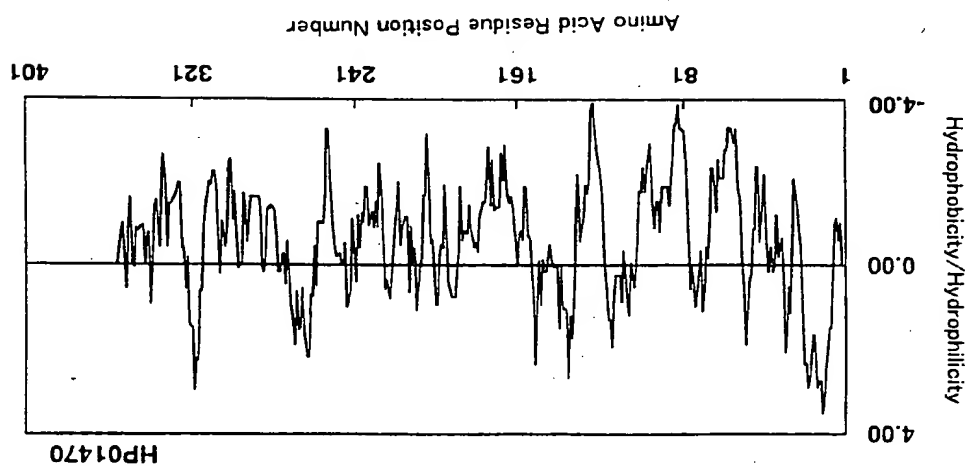


Fig. 31





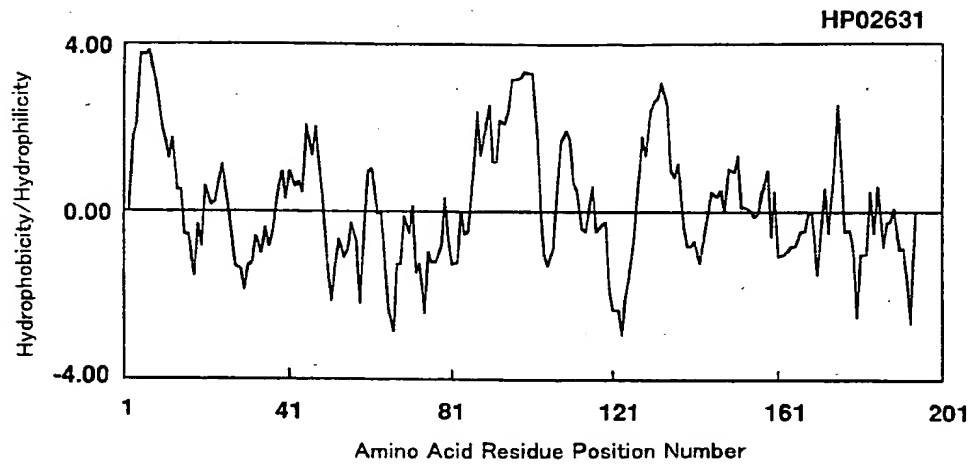


Fig. 33

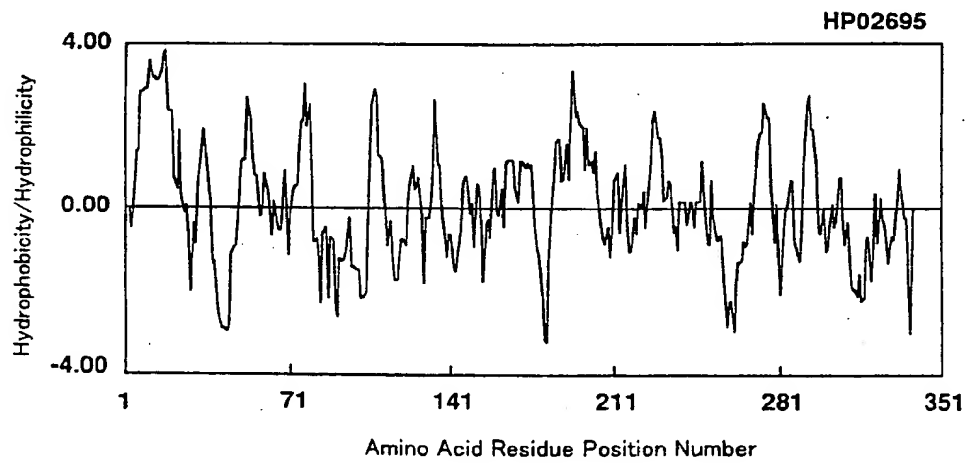


Fig. 34

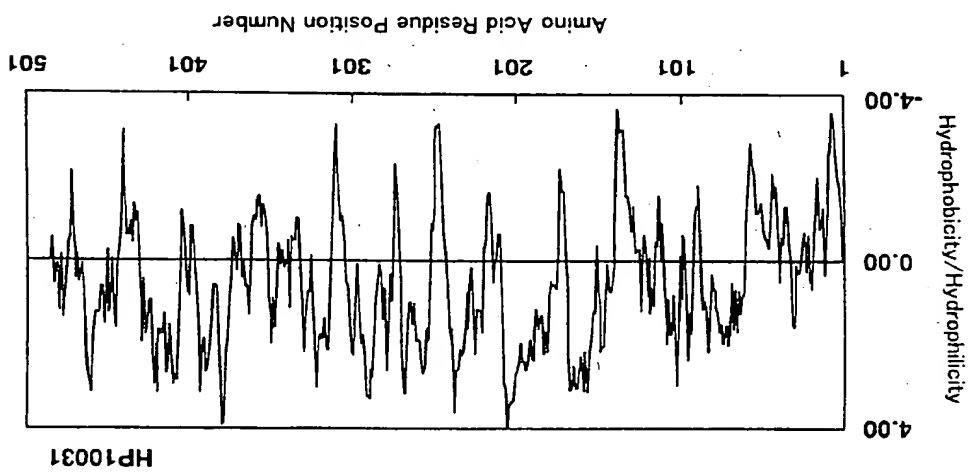


Fig. 35

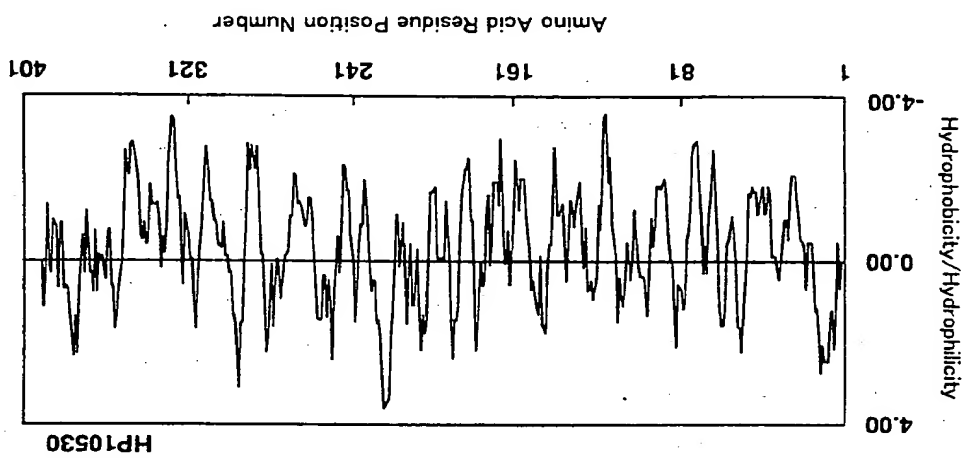


Fig. 36

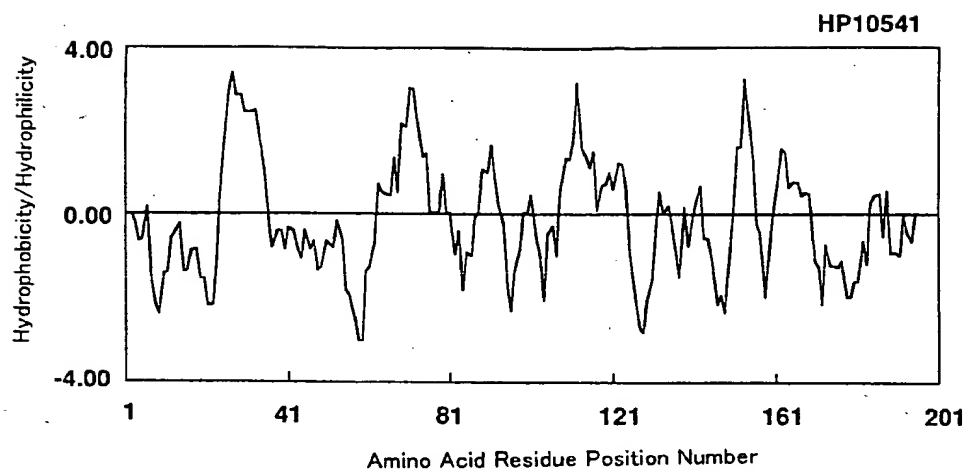


Fig.37

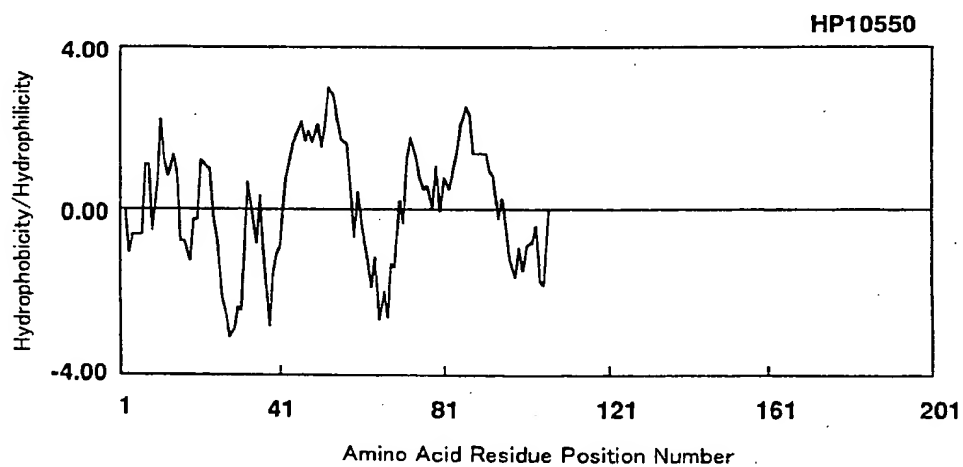


Fig. 38

Fig. 40

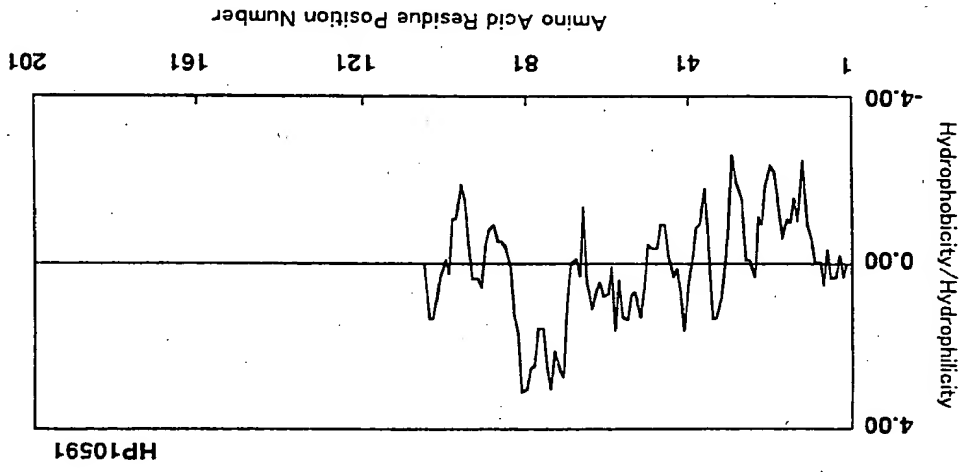
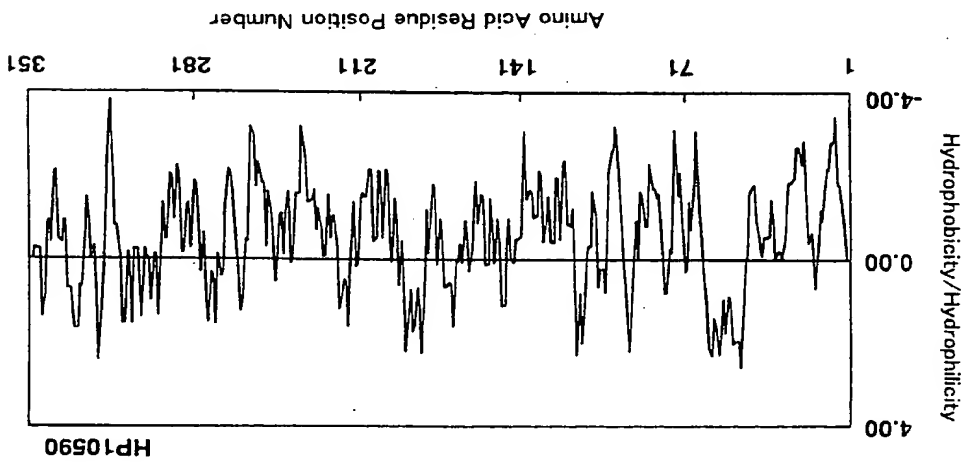


Fig. 39



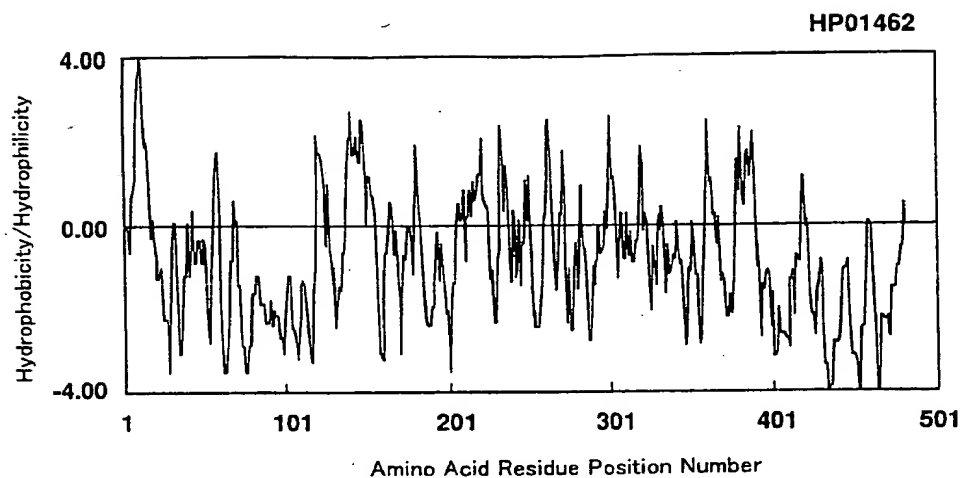


Fig. 41

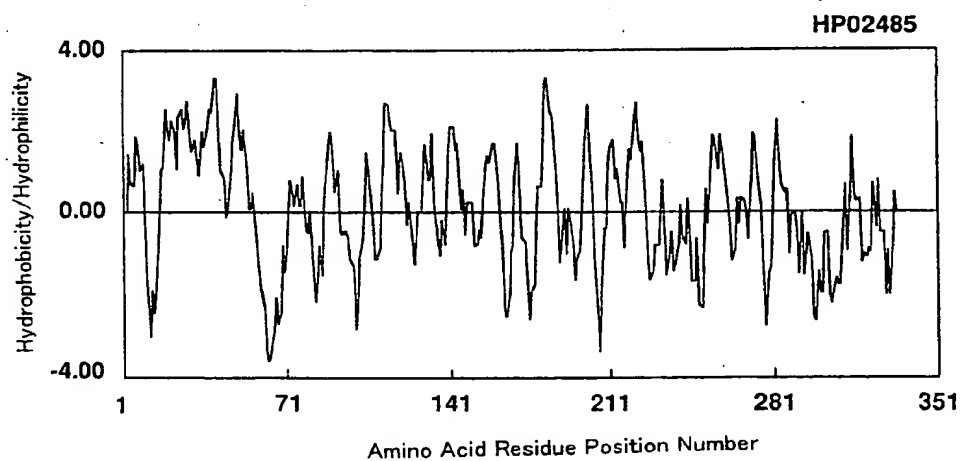


Fig.42

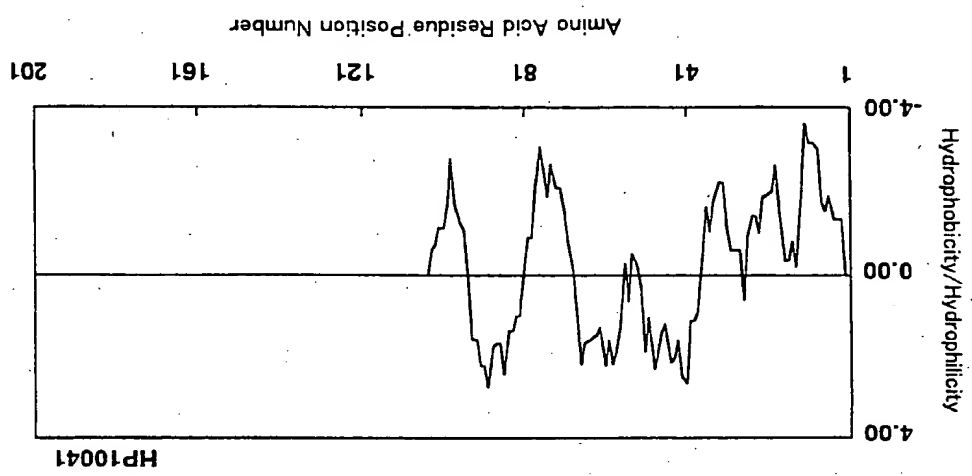


Fig. 44

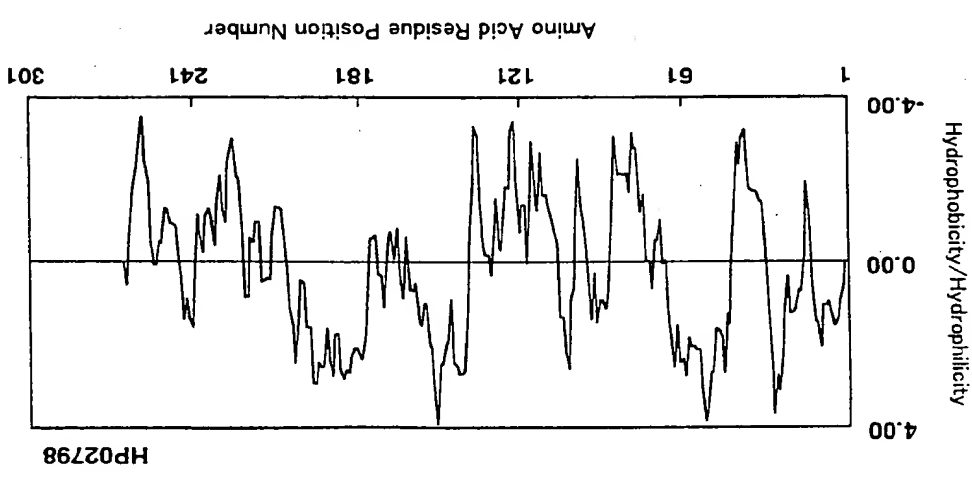


Fig. 43

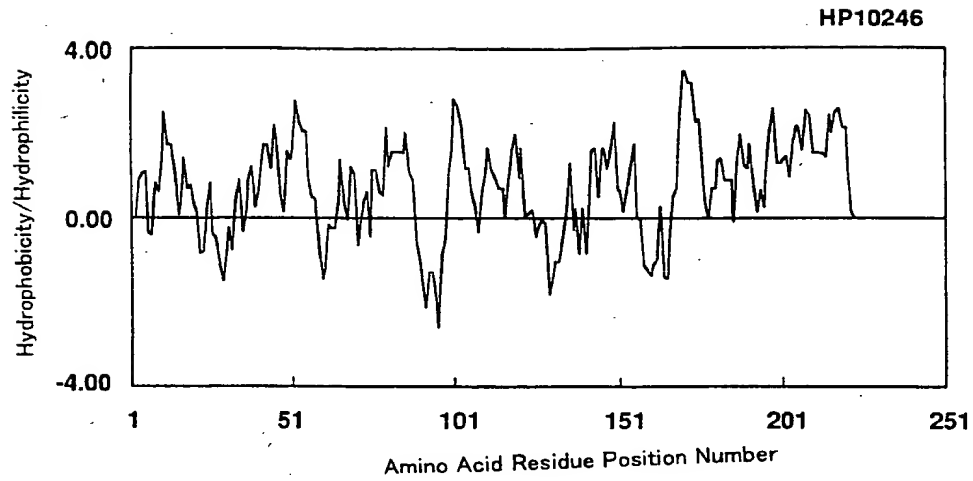


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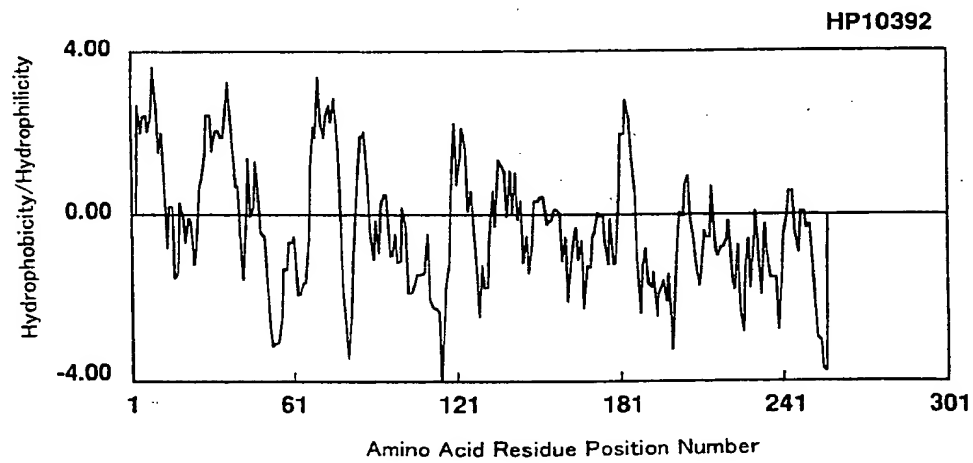


Fig. 46

Fig. 48

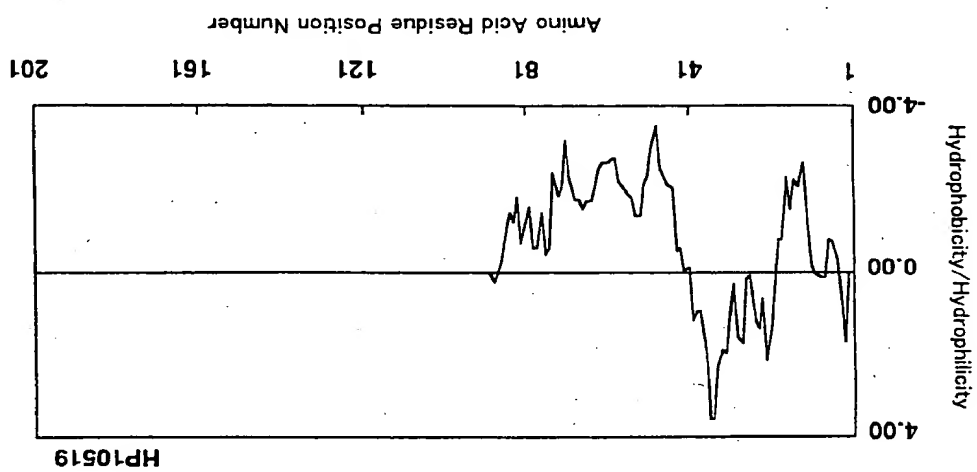
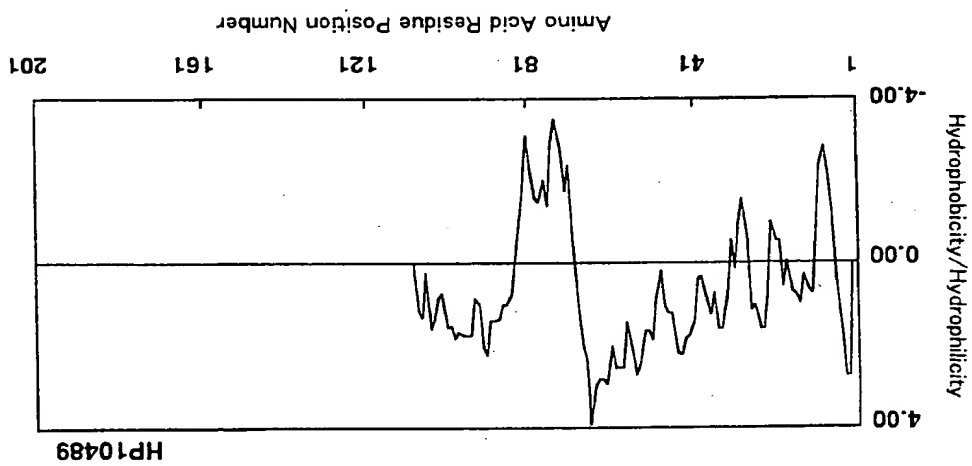


Fig. 47





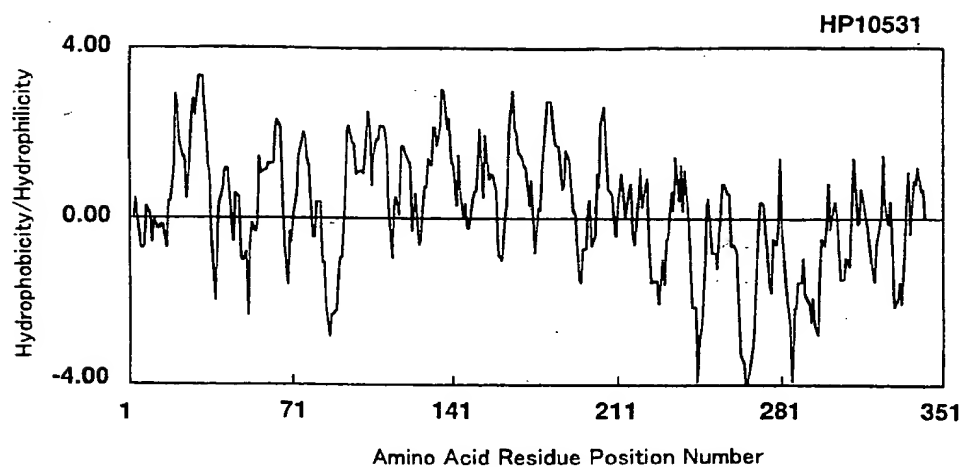


Fig. 49

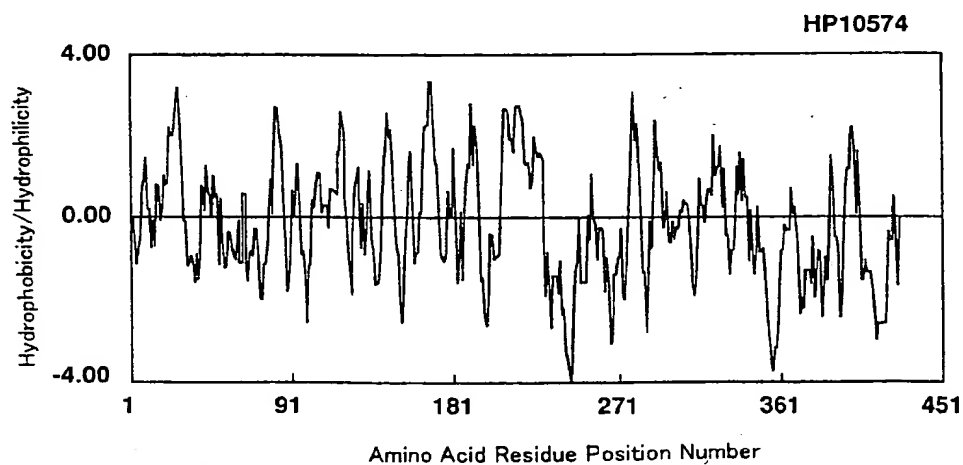


Fig. 50

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## Sequence listing

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&lt;150&gt; JP 10-224105

&lt;151&gt; 1998-08-07

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&lt;150&gt; JP 10-236116

&lt;151&gt; 1998-08-25

&lt;150&gt; JP 10-254736

&lt;151&gt; 1998-09-09

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&lt;150&gt; JP 10-275505

&lt;151&gt; 1998-09-29

25 &lt;160&gt; 150

&lt;170&gt; Windows 95 (Word 98)

&lt;210&gt; 1

30 &lt;211&gt; 125

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 1

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65 70 75 80  
Phe Lys Val Asn Asp Lys Ser Val Gly Gly Ser Phe Tyr Leu Gln Ser  
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Tyr Cys Ile Ala Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn  
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 100 105 110  
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 Tyr Lys Ser Lys Pro Phe Cys Gln Lys Leu Leu Ser Trp Val Lys Ser  
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 130 135 140  
 Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn Trp  
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WO 00/05367

PCT/JP99/03929

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195 200 205  
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 Ser Leu His Tyr Leu Leu Leu Pro Tyr Leu Leu Leu Gly Val Asn Leu  
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His Ser Gly Phe Gln Lys Asn Ser Arg Asp Leu Gly Gln Ile Lys  
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Pro Ser Asn Pro Leu Cys Ser Gln Ser Gly Gln Thr Ser Val Gly Gly  
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165 170 175  
10 Tyr Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser  
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Ser Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly  
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260 265 270  
Lys Pro Lys Glu Thr Tyr Gly Ser Asp Leu Arg Glu Asp Ala Ile  
275 280 285  
25 Ala Pro Gly Ile Ser Glu His Thr Cys Met Arg Ala Asp Ser Lys  
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	gtctggacac ggctctgagc cgtcccaac ctctccggcc tcagctccca ggaagcaaaag	180
	cagattctca acgtgtccaa gctgagccct gaggagctcc agaaagacta tgaacctta	240
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	ttttcacccc tttaacctat tccatctgac atagcaagaa gattatgtga tgaatacagat	180
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	tgtttcaaa tgaagctac agaacctcg cgttactgt tgaagcccaa cagtvgaatc	180
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	gttccactga atgactata gaaagtatga cctatggcaa aaccacacag tgttcaact	480
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atggacaac gcttatttg gaagtccaa ggggctgtcg tgtgtggc cctgacttc 360  
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ctacacaggg aattaaataa aaacttgttt gacacttga ttgaatttct gcaaaatca 240

35



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catctcgcgac tccagagaga ttcagagagc ttgggcctgc aaataaact cagagaaact 300  
ccaactgcctg ctctctctct tgggtatata gcatatgttt gtcatgcac gcaactctgt 360  
gtactcagtc tt 372

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gcgcagctga cctgaacctc cagcagctcg gtggagagaa gcttcgcct ggaatggagc 180  
tttgccagc ctgggaacc cactctgag tccatccaa tccgtact caacatggc 240  
catctgacc caactgttc taagtcaaa cgggtcagcc tgcctcagaa cccccacaa 300  
gtgggggtg ccaaatgaa actgactgac gtccaccct cagatctgac aactacttc 360  
tgcacagtaa acacaccac agattctac acaatgggt tgggtctaat caactact 420  
gtgcctgttc cccccagtaa tccctatgc agtcagatg gacaacctc tgtggagagc 480  
tctaccgac tgaatgagc ctctccgag ggggtccta agccagtga caactgggtg 540  
cgtctgaa atttccac acctctcct ggcagatag ttcagatga ggtgtctgac 600  
cagtcattc tcaacaaact ctccctgacc tccctggga cctacgctg tgtggcacc 660  
aaccaagtag gcaatgacat ctgtgagctg acctctcg tgaccgaac ctccaaagc 720  
cgaatggccg gaactctgat tgggtgtctc ctgggcgtgc tgtgtctgc agttgcctgc 780  
tctcgcctgc tcaagttcaa gaaagagagg gggagagagc ccaagagagc atatgggggt 840  
agtgaacctc gggagatgc catgcctct gggatctcg agcaactg tatagagct 900  
gattcagca aggggttctc ggaagagacc tgcctcgaa gcaaccgtgac gacacaaag 960  
tcaagctcc ctatgtcgt g 981

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Met Ala Lys Tyr Leu Ala Gln Ile Ile Val Met Gly Val Gln Val  
1 5 10 15  
gtg ggc aag gcc ttc gca cgg gcc ttg cgg cag gag ttc gca gcc agc 158  
Val Gly Arg Ala Phe Ala Arg Ala Leu Arg Gln Gln Phe Ala Ala Ser  
20 25 30

10 cgg gcc gca gct gat gcc cga gga cgc gct gga cac cgg tct gca gcc 206  
Arg Ala Ala Asp Ala Arg Gly Arg Ala Gly His Arg Ser Ala Ala  
35 40 45  
gct tcc aac ctg tcc ggc ctg agc ctg cag gag gca cag cag att ctg 254  
Ala Ser Asn Leu Ser Gly Leu Ser Leu Gln Gln Ala Gln Gln Ile Leu  
50 55 60

15 aac gtc tcc aag ctg agc cct gag gag gtc cag aag aac tat gaa cac 302  
Asn Val Ser Lys Leu Ser Pro Gln Gln Val Gln Lys Asn Tyr Gln His  
65 70 75

20 tta ttc aag gtc aat gat aaa tcc gtc ggt gcc tcc ttc tac ctg cag 350  
Leu Phe Lys Val Asn Asp Lys Ser Val Gly Ser Phe Tyr Leu Gln  
80 85 90 95  
tca aag gtc gtc cgc gca aag gag cgc ctg gat gag gaa ctg aaa atc 398  
Ser Lys Val Val Arg Ala Lys Gln Arg Leu Asp Gln Leu Lys Ile  
100 105 110

25 cag gcc cag gag gcc aga gaa aaa ggg cag atg ccc cat acg tgaactgc 450  
Gln Ala Gln Gln Asp Arg Gln Lys Gly Gln Met Pro His Thr  
115 120 125  
gtcccccgc cccaccgcgc cgcctctaat ttaagcttg gtaataaatt tctttctgc 510

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&lt;222&gt; (104)...(499)

&lt;400&gt; 22

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cgcgcgcgc tgggtctgag gacccagag cgcctcacc gcc atg gca ggc atc 115

Met Ala Gly Ile

1

aaa gct ttg att agt ttg tcc ttt gga gga gca atc gga atg atg ttt 163

Lys Ala Leu Ile Ser Leu Ser Phe Gly Gly Ala Ile Gly Leu Met Phe

5 10 15 20

ttg atg ctt gga tgt gcc ctt cca ata tac aac aaa tac tgg ccc etc 211

Leu Met Leu Gly Cys Ala Leu Pro Ile Tyr Asn Lys Tyr Trp Pro Leu

25 30 35

ttt gtt cta ttt ttt tac atc ctt tca cct att cca tac tgc ata gca 259

Phe Val Leu Phe Tyr Ile Leu Ser Pro Ile Pro Tyr Cys Ile Ala

40 45 50

aga aga tta gty gat gat aca gat gct atg agt aac gct tgt aag gaa 307

Arg Arg Leu Val Asp Asp Thr Asp Ala Met Ser Asn Ala Cys Lys Glu

55 60 65

ctt gcc atc ttt ctt aca acg ggc att gtc gty tca gct ttt gga etc 355

Leu Ala Ile Phe Leu Thr Thr Gly Ile Val Val Ser Ala Phe Gly Leu

70 75 80

cct att gta ttt gcc aga gca cat ctg att gag tgg gga gct tgt gca 403

Pro Ile Val Phe Ala Arg Ala His Leu Ile Glu Trp Gly Ala Cys Ala

85 90 95 100

ctt gtt ctc aca gga aac aca gtc atc ttt gca act ata cta ggc ttt 451

Leu Val Leu Thr Gly Asn Thr Val Ile Phe Ala Thr Ile Leu Gly Phe

105 110 115

ttc ttg gtc ttt gga agc aat gac gac ttc agc tgg cag cag tgg tga 500

Phe Leu Val Phe Gly Ser Asn Asp Asp Phe Ser Trp Glu Trp

120 125 130

aagaattac tgaactatg tcaaatggac ttcctgtcat ttgttgcca ttaacgaca 560

caggagatgg ggcagttaat gctgaatggt atagcaagcc ttctgggggt atttaggtg 620

ctcccttc actttttg taagctact attttcacg agactgtcg aagattaa 680

aggattttct cttttg 697

&lt;210&gt; 23

&lt;211&gt; 1619

&lt;212&gt; DNA

5 &lt;213&gt; Homo sapiens

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (287)...(1015)

10 &lt;400&gt; 23

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tgggtttgag taactgtgag gacccagagc tctgacaca ggcgtggcc caccagaccg 120

gtacacagc ggcagcggtt agggctggg agcggagc ctggcctgt cctagagctc 180

ggcagagcg tgcgcctgt cgtcccccgc cccagctcag caaacgcgc cgcgggggc 240

gccccctc tgcgtgtct ctcagatggt ctcagctca ggggac atg ggc aag 295

Met Ala Lys

1

cac gag cag atc ctg gtc ctc gat ccg ccc aca gac ctc aaa ttc aaa 343

His Glu Gln Ile Leu Val Leu Asp Pro Thr Asp Leu Lys Phe Lys

20 5 10 15

ggc ccc ttc aca gat gta gtc act aca aat ctt aaa ttg cga aat cca 391

Gly Pro Phe Thr Asp Val Val Thr Thr Asn Lys Leu Arg Asn Pro

20 25 30 35

tcg gat aga aaa gty tgt ttc aaa gty aag act aca gca cct cgc egg 439

Ser Asp Arg Lys Val Cys Phe Lys Val Lys Thr Thr Ala Pro Arg Arg

25 40 45 50

tac tgt gty agg ccc aac agt gga att att gac cca ggg tca act gty 487

Tyr Cys Val Arg Pro Asn Ser Gly Ile Ile Asp Pro Gly Ser Thr Val

55 60 65

act gtt tca gta atg cta cag ccc ttt gat tat gat ccg aat gaa aag 535

Thr Val Ser Val Met Leu Gln Pro Phe Asp Tyr Asp Pro Asn Glu Lys

70 75 80

agt aac cac aag ttt atg gta cag aca att ttt gct cca cca aac act 583

Ser Lys His Lys Phe Met Val Gln Thr Ile Phe Ala Pro Pro Asn Thr

85 90 95

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100 tca gat atg gaa gct gfg' tgg aaa gag gaa aac cct gat gaa tta atg 631  
Ser Asp Met Glu Ala Val Trp Lys Glu Ala Lys Pro Asp Glu Leu Met  
105 110 115  
gat tcc aaa tgg aga tgc gta ttt gaa atg ccc aat gaa aat gat aaa 679  
Asp Ser Lys Leu Arg Cys Val Phe Glu Met Pro Asn Glu Asn Asp Lys  
120 125 130  
ttg aat gat atg gaa cct agc aaa gct gtc cca ctg aat gaa tct aag 727  
Leu Asn Asp Met Glu Pro Ser Lys Ala Val Pro Leu Asn Ala Ser Lys  
135 140 145  
caa gat gga cct atg cca aaa cca agc agt gtc tca ctt aat gat acc 775  
Gln Asp Gly Pro Met Pro Lys Pro His Ser Val Ser Leu Asn Asp Thr  
150 155 160  
gaa aca agg aaa cta atg gaa gag tgt aaa aga ctt cag gga gaa atg 823  
Glu Thr Arg Lys Leu Met Glu Glu Cys Lys Arg Leu Glu Gly Glu Met  
165 170 175  
atg aag cta tca gaa gaa aat cgg cnc ctg aga gat gaa ggt tta agg 871  
Met Lys Leu Ser Glu Glu Asn Arg His Leu Arg Asp Glu Gly Leu Arg  
180 185 190 195  
ctc aga aag gta gaa cat tgg gat aaa cct gga tca acc tca act gaa 919  
Leu Arg Lys Val Ala His Ser Asp Lys Pro Gly Ser Thr Ser Thr Ala  
200 205 210  
tcc ttc aga gat aat gto acc agt cct ctt cct tca ctt ctt gtc gta 967  
Ser Phe Arg Asp Asn Val Thr Ser Pro Leu Pro Ser Leu Leu Val Val  
215 220 225  
att gaa ggc att ttc att gga ttc ttt cta ggg aaa ttc atg ttg 1012  
Ile Ala Ala Ile Phe Ile Gly Phe Phe Leu Glu Lys Phe Ile Leu  
230 235 240  
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gatttgta octaccatt catgtagt atggccacg gtaaccatt ttctgtgt 1130  
acagtgat atnagcttg ccttaatga tctctacgg ttagaaca caataaac 1190  
aaactgag gtaactgac aggttgata ttaacagac atcaatgaa gatgaggt 1250  
gcaatgag tcttaatga aatcaataa taagaatg ttcttctt gtgtgttaa 1310  
taagaatga agaatgta agagtctgt aatgttat ttaataacc cttaaat 1370  
tatctgtgc tgtacctct tgaatatga ttatattaga ttgctaacc caatcatca 1430  
ggaatgcaa agagratct ctgggaaa tggtagctct taagatgaa atttctctc 1490

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ttaacagat 1619  
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Met Phe Val Pro Cys Gly Glu Ser Ala Pro Asp Leu Ala Gly Phe  
1 5 10 15  
acc ctc cta atg cca gaa gta tct gtc gga aat gtc ggc cag ctt gaa 157  
Thr Leu Leu Met Pro Ala Val Ser Val Gly Asn Val Gly Glu Leu Ala  
20 25 30  
atg gat ctg att att tct aca ctg aat atg tct aag att ggt tac ttc 205  
Met Asp Leu Ile Ile Ser Thr Leu Asn Met Ser Lys Ile Gly Tyr Phe  
35 40 45  
tat acc gat tgt ctt gfg cca atg gtc gga aac aat cca tat gcg acc 253  
Tyr Thr Asp Cys Leu Val Pro Met Val Gly Asn Asn Pro Tyr Ala Thr  
50 55 60  
aca gaa gga aat tca aca gaa ctt agc ata aat gct gaa gfg tat tca 301  
Thr Glu Gly Asn Ser Thr Glu Leu Ser Ile Asn Ala Glu Val Tyr Ser  
65 70 75  
ttg cct tca aga aag ctg gfg gct cta cag tta aga tcc att ttt att 349  
Leu Pro Ser Arg Lys Leu Val Ala Leu Glu Leu Arg Ser Ile Phe Ile  
80 85 90 95  
aag tat aaa tca aag cca ttc tgt gaa aaa ctg ctt tcc tgg gfg aaa 397  
Lys Tyr Lys Ser Lys Pro Phe Cys Glu Lys Leu Leu Ser Trp Val Lys  
100 105 110

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5 agc agt ggc tgt gcc aga gtc att gtt ctt tcg agc agt cat tca tat 445  
 Ser Ser Gly Cys Ala Arg Val Ile Val Leu Ser Ser Ser His Ser Tyr  
 115 120 125  
 cag cgt aat gat cgt cag ctt cgt agt act ccc ttc cgg tac cta ctt 493  
 Gln Arg Asn Asp Leu Gln Leu Arg Ser Thr Pro Phe Arg Tyr Leu Leu  
 130 135 140  
 aca cct tcc atg caa aaa agt gtt caa aat aaa ata aag agc att aac 541  
 Thr Pro Ser Met Gln Lys Ser Val Gln Asn Lys Ile Lys Ser Leu Asn  
 145 150 155  
 10 tgg gaa gaa atg gaa aaa agc cgg tgc att cct gaa ata gat gat tcc 589  
 Trp Glu Glu Met Glu Lys Ser Arg Cys Ile Pro Glu Ile Asp Asp Ser  
 160 165 170 175  
 gag ttt tgt atc cgc att ccg gga gga ggt atc aca aaa aca ctc tat 637  
 Glu Phe Cys Ile Arg Ile Pro Gly Gly Ile Thr Lys Thr Leu Tyr  
 180 185 190  
 gat gaa agc tgt tct aaa gaa atc caa atg gca gtt ctg ctg aaa ttt 685  
 Asp Glu Ser Cys Ser Lys Glu Ile Gln Met Ala Val Leu Leu Lys Phe  
 195 200 205  
 gtt tca gaa ggg gac aac atc cca gat gca tta ggt ctt gtt gag tat 733  
 Val Ser Glu Gly Asp Asn Ile Pro Asp Ala Leu Gly Leu Val Glu Tyr  
 210 215 220  
 ctt aat gag tgg ctt cag ata ctc aaa cca cca ctt agc gat gac ccc aca 781  
 Leu Asn Glu Trp Leu Gln Ile Leu Lys Pro Leu Ser Asp Asp Pro Thr  
 225 230 235  
 25 gta tct gcc tca cgg tgg aaa ata cca agt tct tgg aga tta ctc ttt 829  
 Val Ser Ala Ser Arg Trp Lys Ile Pro Ser Ser Trp Arg Leu Leu Phe  
 240 245 250 255  
 ggc agt ggt ctt ccc cct gca ctt ttc tgatctaatt tctgtttat acct 880  
 Gly Ser Gly Leu Pro Pro Ala Leu Phe  
 260  
 30 tatecccaaa acacttacta ccaacacgc tgtaaactat tctatacaaa aaaaatgtat 940  
 gatctgtat taggaatta ctttccagt aaatacaaa gaaaaagt taagggtc 1000  
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 ctaagt 1066

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 Gly Ser Arg Leu Ser Gln Pro Phe Glu Ser Tyr Ile Thr Ala Pro Pro  
 15 5 10 15  
 ggt acc gcc gcc cgc ccc gcc aaa cct gcg ccc cca gct aca ccc gga 152  
 Gly Thr Ala Ala Ala Pro Ala Lys Pro Ala Pro Ala Thr Pro Gly  
 20 20 25 30  
 gag ccg acc tcc cca gca gaa cac cgc ctg ttg aag acc tgc tgg agc 200  
 Ala Pro Thr Ser Pro Ala Glu His Arg Leu Leu Lys Thr Cys Trp Ser  
 35 40 45  
 tgt cgc gtg ctt tct ggg ttg ggg ctg atg ggg gcg ggc ggg tac gtg 248  
 Cys Arg Val Leu Ser Gly Leu Met Gly Ala Gly Tyr Val  
 50 55 60 65  
 25 tac tgg gtg gca cgg aag ccc atg aag atg gga tac ccc ccg agt cca 296  
 Tyr Trp Val Ala Arg Lys Pro Met Lys Met Gly Tyr Pro Pro Ser Pro  
 70 75 80  
 tgg acc att acg cag atg gtc atc ggc ctc agc att gcc acc tgg ggt 344  
 Trp Thr Ile Thr Gln Met Val Ile Gly Leu Ser Ile Ala Thr Trp Gly  
 85 90 95  
 atc gtt gtc atg gca gac ccc aaa ggg aag gcc tac cgc gtt gtt t 390  
 Ile Val Val Met Ala Asp Pro Lys Gly Lys Ala Tyr Arg Val Val  
 100 105 110  
 gaagtaacca ccaagtgaac tgattctgt cctgtccct ttccccgtga ccaacacgc 450  
 aggcacggaa ttaattgggt gttctggaca gaaacttga catggacaga catcactact 510

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gtggaatactaa caagactgag aagaaatcgt tatgttgcga ttctcttgct atggagtgt	570
tgtggccttc acagatttca caggaaacaa taatctcttc agagaggt	618
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cggtcaccgg cccgaagata ctcaacgggg ctatagtgtt gcttcggggg cgggagacgga	120
ggtgagcggg agctatggcc gcgagccccc gccggccctt cctccagcgc cctgcggacc	180
ccgcagaagg cgtctagcctc cctagccccc aaaaacatat cgattttct cgtcttggga	240
aaggggagct cctatagat cctctgctcc aataggaac tccggccttc cctgcctga	300
cctggaaact ctgggaaggc tgcagaataa gtgcgccttc tgcgtccga cggagggacc	360
aggtcttggg agtagtccc tctgttccga caggtgcgac acttggcgt cc atg ctt	418
Met Leu	
1	
gcc ggt gcc ggg agg cct ggc ctc ccc cag ggc cgc cag ctc tgc tgg	466
Ala Gly Ala Gly Arg Pro Gly Leu Pro Gln Gly Arg His Leu Cys Trp	
5 10 15	
ctg ctc tgt gct ttc acc tta aag ctc tgc caa gaa gag gct ccc gtc	514
Leu Leu Cys Ala Phe Thr Leu Lys Leu Cys Gln Ala Gln Ala Pro Val	
20 25 30	
cag gaa gag aag ctg tca gca agc acc tca aat ttg cca tgc tgg ctg	562
Gln Gln Gln Lys Leu Ser Ala Ser Thr Ser Asn Leu Pro Cys Trp Leu	
35 40 45 50	
gtg gaa gag tct gtc gta gca gaa gag tgc tct cca tgc tct aat ttc	610
Val Gln Gln Phe Val Ala Gln Gln Cys Ser Pro Cys Ser Asn Phe	
55 60 65	
cgg gct aaa act acc cct gag tgt ggt ccc aca gga tat gta gag aaa	658
Arg Ala Lys Thr Thr Pro Gln Cys Gly Pro Thr Gly Tyr Val Gln Lys	

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atc aca tgc agc tca tct aag aga aat gag ttc aaa agc tgc cgc tca	706
Ile Thr Cys Ser Ser Ser Lys Arg Asn Gln Phe Lys Ser Cys Arg Ser	
85 90 95	
gct ttg atg gaa caa cgc tta ttt tgg aag ttc gaa ggg gct gtc gtc	754
Ala Leu Met Gln Gln Arg Leu Phe Thr Lys Phe Gln Gly Ala Val Val	
100 105 110	
tgt gtc gcc ctg atc ttc gct tgt ctt gtc atc att cgt cag cga caa	802
Cys Val Ala Leu Ile Phe Ala Cys Leu Val Ile Ile Arg Gln Arg Gln	
115 120 125 130	
ctg gac aga aag gct ctg gaa aag gtc cgg aag caa atc gag tcc ata	850
Leu Asp Arg Lys Ala Leu Gln Lys Val Arg Lys Gln Ile Gln Ser Ile	
135 140 145	
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aaatggaact atttgaacte ttggtcttt ggaacctgtt ggttgaatcc cctttccc	970
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tcctggaga accatgtccc gcaactaag gtaactgcag gcaacactg ctggccaaga	240
ggagctgtgt tttagaatat ctgtgaatgt tgggaagagg aatgccagag ctggcgctg	300
aaatataccc aaccaagaga aatctcag atg gac ttt ctg gtc ctc ttc ttg	354
Met Asp Phe Leu Val Leu Phe Leu	
1 5	
ttc tac ctg gct tcc gtc ctg atg ggt ctt gtc ctc atc tgc tgc tgc	402

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Phe Tyr Leu Ala Ser Val Leu Met Gly Leu Val Leu Ile Cys Val Cys  
 10 15 20  
 tgg aaa acc cat agc ttg aaa ggc ctg gcc agg gga gca cag ata 450  
 Ser Lys Thr His Ser Leu Lys Gly Leu Ala Arg Gly Gly Ala Gln Ile  
 25 30 35 40  
 ttt tcc tgt ata att cca gaa tgt ctt cag aga gcc gtg cat gga tgg 498  
 Phe Ser Cys Ile Ile Pro Glu Cys Leu Gln Arg Ala Val His Gly Leu  
 45 50 55  
 ctt cat tac ctt ttc cat acg aga aac cac acc ttc att gtc ctg cac 546  
 Leu His Tyr Leu Phe His Thr Arg Asn His Thr Phe Ile Val Leu His  
 60 65 70  
 ctg gtc ttg caa ggg atg gtt tat act gag tac acc tgg gaa gta ttt 594  
 Leu Val Leu Gln Gly Met Val Tyr Thr Glu Tyr Thr Trp Glu Val Phe  
 75 80 85  
 ggc tac tgt cag gag ctg gag ttg tcc ttg cat tac ctt ctt ctg ccc 642  
 Gly Tyr Cys Gln Glu Leu Glu Leu Ser Leu His Tyr Leu Leu Leu Pro  
 90 95 100  
 tat ctg ctg cta ggt gta aac ctg ttt ttt ttc acc ctg act tgt gga 690  
 Tyr Leu Leu Leu Gly Val Asn Leu Phe Phe Thr Leu Thr Cys Gly  
 105 110 115 120  
 acc aat cct gcc att ata aca aca gca aat gaa tta tta ttt ctt cat 738  
 Thr Asn Pro Gly Ile Ile Thr Lys Ala Asn Glu Leu Leu Phe Leu His  
 125 130 135  
 gtt tat gaa ttt gat gaa gtg atg ttt cca aag aac gtg agg tgc tat 786  
 Val Tyr Glu Phe Asp Glu Val Met Phe Pro Lys Asn Val Arg Cys Ser  
 140 145 150  
 act tgt gat tta agg aac cca gct cga tcc aag cac tgc agt gtg tgt 834  
 Thr Cys Asp Leu Arg Lys Pro Ala Arg Ser Lys His Cys Ser Val Cys  
 155 160 165  
 aac tgg tgt gtg cac cgt ttc gcc cat cac tgt gtt tgg gtg aac aac 882  
 Asn Trp Cys Val His Arg Phe Asp His His Cys Val Trp Val Asn Asn  
 170 175 180  
 tgc atc ggg gcc tgg aac atc agg tac ttc ctc atc tac gtc ttg acc 930  
 Cys Ile Gly Ala Trp Asn Ile Arg Tyr Phe Leu Ile Tyr Val Leu Thr  
 185 190 195 200

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ttg acg gcc tgg gct gcc acc gtc att gtg agc acc act ttt ctg 978  
 Leu Thr Ala Ser Ala Ala Thr Val Ala Ile Val Ser Thr Thr Phe Leu  
 205 210 215  
 gtc cac ttg gtg atg tta tta tta tta tta tta tta tta tta tta tta 1026  
 Val His Leu Val Val Met Ser Asp Leu Tyr Gln Glu Thr Tyr Ile Asp  
 220 225 230  
 gac ctt gga cac ctc cat gtt atg gac acg gtc ttt ctt att cag tac 1074  
 Asp Leu Gly His Leu His Val Met Asp Thr Val Phe Leu Ile Gln Tyr  
 235 240 245  
 ctg ttc ctg act ttt cca cgg att gtc ttc atg ctg ggc ttt gtc gtg 1122  
 Leu Phe Leu Thr Phe Pro Arg Ile Val Phe Met Leu Gly Phe Val Val  
 250 255 260  
 GTT CTG AGC TTC CTC CTG GGT GGC TAC CTG TTT TTT GTC CTG TAT CTG 1170  
 Val Leu Ser Phe Leu Leu Gly Gly Tyr Leu Leu Phe Val Leu Tyr Leu  
 265 270 275 280  
 gcg gcc acc aac cag act act aac gag tgg tac aga ggt gac tgg gcc 1218  
 Ala Ala Thr Asn Gln Thr Thr Asn Glu Trp Tyr Arg Gly Asp Trp Ala  
 285 290 295  
 tgg tgc cag cgt tgt ccc ctt gtg gcc tgg cct cag tca gca gag ccc 1266  
 Trp Cys Gln Arg Cys Pro Leu Val Ala Trp Pro Pro Ser Ala Glu Pro  
 300 305 310  
 caa gtc cac cgg aac att cac tcc cat ggg ctt cgg agc aac ctt caa 1314  
 Gln Val His Arg Asn Ile His Ser His Gly Leu Arg Ser Asn Leu Gln  
 315 320 325  
 gag atc ttt cta cct gcc ttt cca tgt cat gag agg aag aca gaa 1362  
 Glu Ile Phe Leu Pro Ala Phe Pro Cys His Glu Arg Lys Lys Gln Glu  
 330 335 340  
 tgcacagtgt atgactgct ttgagatgta gttcccggtt attaacatc gtggatcc 1420  
 tegttttcaa ag 1432  
 <210> 28  
 <211> 601  
 <212> DNA  
 <213> Homo sapiens  
 <220>

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<221> CDS  
<222> (62)...(355)

<400> 28  
atcgacacat agcgacttgg tgggcgcgtc caatgatgac tgggggatac ccgaagataa 60  
c atg act aaa aag aag cgg gag aat ctg ggc gtc gct cta gag atc gat 109  
Met Thr Lys Lys Arg Gln Asn Leu Val Ala Leu Gln Ile Asp  
1 5 10 15  
ggg cta gag gag aag ctg tcc cag tgt cgg aga gac ctg gag ggc gtc 157  
Gly Leu Gln Gln Lys Leu Ser Gln Cys Arg Arg Asp Leu Gln Ala Val  
20 25 30  
aac tcc aga ctc cac agc cgg gag ctg agc cca gag gcc agg agg tcc 205  
Asn Ser Arg Leu His Ser Arg Gln Leu Ser Pro Gln Ala Arg Arg Ser  
35 40 45  
ctg gag aag gag aaa aac agc cta atg aac aaa gcc tcc aac tac gag 253  
Leu Gln Lys Gln Lys Asn Ser Leu Met Asn Lys Ala Ser Asn Tyr Gln  
50 55 60  
aag gaa ctg aag ttt ctt cgg caa gag aac cgg aag aac atg ctg ctc 301  
Lys Gln Leu Lys Phe Leu Arg Gln Gln Asn Arg Lys Asn Met Leu Leu  
65 70 75 80  
tct gtc gcc atc ttt atc ctc ctg aag ctc gtc tat gcc tac tgg acc 349  
Ser Val Ala Ile Phe Ile Leu Leu Thr Leu Val Tyr Ala Tyr Trp Thr  
85 90 95  
atg tgaagctggc acttcccac aaccagaca ggttccact tggccct 400  
Met  
25  
tgatcagat caagcagaa cttaagcct caatagAAC aagtgctgg gtcgtccccc 460  
tcccaacctt gtttcacagc atggttctt ggcggccag gcttgcctc ccgggcctgc 520  
tgggggttc ccgggtccca gaagacatg gtgcgtgcc ctccctagg caaaggagaa 580  
30 ggcataaag acacaaagct g 601

<210> 29  
<211> 585  
<212> DNA  
<213> Homo sapiens

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<220>  
<221> CDS  
<222> (78)...(452)

<400> 29  
actaaccttc ggcctgcagc cgcgggggcg ccggggaat ccagagtga tctgaaatc 60  
gcaggtcag taagacc atg gct aag tcc tgg atg tct aag ggt tgc ttt 110  
Met Ala Thr Ser Ser Met Ser Lys Gly Cys Phe  
1 5 10  
gtt ttt aag cca aac tcc aaa aag aga aag atc tct ctg cca ata gag 158  
Val Phe Lys Pro Asn Ser Lys Lys Arg Lys Ile Ser Leu Pro Ile Gln  
15 20 25  
gac tat ttt aac aaa ggg aaa aat gag cct gag gac agt aag ctt cga 206  
Asp Tyr Phe Asn Lys Gly Lys Asn Gln Pro Gln Asp Ser Lys Leu Arg  
30 35 40  
ttc gaa act tat cag ttg ata tgg cag cag atg aaa tct gaa aat gag 254  
Phe Gln Thr Tyr Gln Leu Ile Trp Gln Gln Met Lys Ser Gln Asn Gln  
45 50 55  
cga cta caa gag gaa tta aat aaa aac ttg ttt gac aat ctg att gaa 302  
Arg Leu Gln Gln Gln Leu Asn Lys Asn Leu Phe Asp Asn Leu Ile Gln  
60 65 70 75  
ttt ctg caa aaa tca cat tct gga ttc cag aag aat tca aga gac ttg 350  
Phe Leu Gln Lys Ser His Ser Gly Phe Gln Lys Asn Ser Arg Asp Leu  
80 85 90  
ggc ggt caa ata aaa atc aga gaa att cca act gct gct ctt gtt ctt 398  
Gly Gly Gln Ile Lys Leu Arg Gln Ile Pro Thr Ala Ala Leu Val Leu  
95 100 105  
ggt ata tat gag tat gtt tgt tca tgc atg cat ctc tgt gta ttt cgt 446  
Gly Ile Tyr Ala Tyr Val Cys Ser Cys Met His Leu Cys Val Phe Arg  
110 115 120  
ttt taattttt tttaattgtt agaataatg aaggaactgt tttagtgagc c 500  
Phe  
25  
tatattgct ctcttatitg taacaataaa ccaactatag ttatatatc atatttcaa 560  
35 aaaccaataa aaattcctta tcttt 585

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6	<210> 30	115	120	125	Ser Asp Thr Gly Thr Tyr Leu Cys Gln Val Asn Asn Pro Pro Asp Phe	491		
	<211> 1100				tac acc aat ggg ttg ggg cta atc aac ctt act gtg ctg gtt ccc ccc			
	<212> DNA				Tyr Thr Asn Gly Leu Gly Leu Ile Asn Leu Thr Val Leu Val Pro Pro			
	<213> Homo sapiens	130	135	140	145			
	<220>							
	<221> CDS							
	<222> (57)...(1040)							
10	<400> 30	150	155	160	Ser Asn Pro Leu Cys Ser Gln Ser Gly Gln Thr Ser Val Gly Gly Ser	539		
	agacgaacct tgaacgacca cctggacaga gcaggacagg acggcgggac gcggcc atg	165	170	175	act gca ctg aga tgc agc tct tcc gag ggg gct cct aag cca gtg tac	587		
					Thr Ala Leu Arg Cys Ser Ser Glu Gly Ala Pro Lys Pro Val Tyr			
					acc tgg gtg cgt ctt gga act ttt cct aca cct tct cct ggc agc atg	635		
					Asn Trp Val Arg Leu Gly Thr Phe Pro Thr Pro Ser Pro Gly Ser Met			
15	gcc gag ctc ccg ggg ccc ttt ctc tgc ggg gcc ctg cta ggc ttc ctg	180	185	190	ggt cea gat gag gtg tct ggc cag ctc att ctc acc aac ctc tcc ctg	683		
	Ala Glu Leu Pro Gly Pro Phe Leu Cys Gly Ala Leu Leu Gly Phe Leu				Val Gln Asp Glu Val Ser Gly Gln Leu Ile Leu Thr Asn Leu Ser Leu			
		5	10	15				
	tgc ctg agt ggg ctg gcc gtg gag gtg aag gta ccc aca gag ccg ctg	195	200	205	acc tcc tcg ggc acc tac cgc tgt gtg gcc acc aac cag atg ggc agt	731		
	Cys Leu Ser Gly Leu Ala Val Glu Val Lys Val Pro Thr Glu Pro Leu				Thr Ser Ser Gly Thr Tyr Arg Cys Val Ala Thr Asn Gln Met Gly Ser			
		20	25	30	210	215	220	225
20	agc acg ccc ctg ggg aag aca gcc gag ctg acc tgc acc tac agc acg				gca tcc tgt gag ctg acc ctc tct gtg acc gaa ccc tcc cca ggc aga			
	Ser Thr Pro Leu Gly Lys Thr Ala Glu Leu Thr Cys Thr Tyr Ser Thr				Ala Ser Cys Glu Leu Thr Leu Ser Val Thr Glu Pro Ser Gln Gly Arg			
		35	40	45	230	235	240	
	tgc gtg gga gac agc ttc gcc ctg gag tgg agc ttt gtg cag cct ggg				gtg gcc gga gct ctg att ggg gtg ctc ctg ggc gtg ctg ttg ctg tca			
	Ser Val Gly Asp Ser Phe Ala Leu Glu Trp Ser Phe Val Gln Pro Gly				Val Ala Gly Ala Leu Ile Gly Val Leu Leu Gly Val Leu Leu Ser			
25	aaa ccc atc tct gag tcc cat cca atc ctg tac ttc acc aat ggc cat	245	250	255	ggt gct gcg ttc tgc ctg gtc agg ttc cag aaa gag agg ggg aag aag			
	Lys Pro Ile Ser Glu Ser His Pro Ile Leu Tyr Phe Thr Asn Gly His				Val Ala Ala Phe Cys Leu Val Arg Phe Gln Lys Glu Arg Gly Lys Lys			
		65	70	75	260	265	270	
	ctg tat cca act ggt tct aag tca aag cgg gtc agc ctg ctt cag aac				ccc aag gag aca tat ggg ggt agt gac ctt cgg gag gat gcc atc gct			
	Leu Tyr Pro Thr Gly Ser Lys Ser Lys Arg Val Ser Leu Leu Gln Asn				Pro Lys Glu Thr Tyr Gly Gly Ser Asp Leu Arg Glu Asp Ala Ile Ala			
		85	90	95	275	280	285	
30	ccc ccc aca ctg ggg gtg gcc aca ctg aaa ctg act gac gtc cac ccc				cct ggg atc tct gag cac act tgt atg agg gct gat tct agc aag ggg			
	Pro Thr Val Gly Val Ala Thr Leu Lys Leu Thr Asp Val His Pro				Pro Gly Ile Ser Glu His Thr Cys Met Arg Ala Asp Ser Ser Lys Gly			
		100	105	110	290	295	300	305
35	tea gat act gga acc tac ctc tgc caa gtc aac aac cca cca gat ttc							



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ttc ctg gaa aga ccc tct ggc agc acc gtc acg acc aag tcc 1019  
 phe leu glu arg pro ser ser ala ser thr thr thr lys ser 310 315 320  
 aag ctc cct atg gtc gtc tgactctcc cgatccctga gggcgggtgag ggg 1070  
 lys leu pro met val 325  
 gaacatcaat aactaagtc tctgggtgacc 1100  
 <210> 31  
 <211> 313  
 <212> PRT  
 <213> Homo sapiens  
 <400> 31  
 Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg Gly  
 1 5 10 15  
 Trp Ser Thr Asp Glu Ala Asn Thr Tyr Phe Lys Glu Trp Thr Cys Ser  
 20 25 30  
 Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Glu Ile Lys Asp Glu Cys  
 35 40 45  
 Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Glu Asn Gly Val  
 50 55 60  
 Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Trp Thr  
 65 70 75 80  
 Leu Val Ala Ser Val His Glu Asn Asp Met Arg Gly Lys Cys Thr Val  
 85 90 95  
 Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Gln  
 100 105 110  
 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Glu Ala  
 115 120 125  
 Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala  
 130 135 140  
 Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His  
 145 150 155 160  
 Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Thr Gly Phe Leu

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Gln Thr Leu Gly His Asn Leu Phe Gly Ile Tyr Gln Lys Tyr Pro Val  
 165 170 175  
 180 185 190  
 Lys Tyr Gly Glu Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro  
 195 200 205  
 Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser  
 210 215 220  
 Pro Tyr Gly Gln Arg Glu Phe Thr Ala Gly Phe Val Gln Phe Arg Val  
 225 230 235 240  
 Phe Asn Asn Glu Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val  
 245 250 255  
 Thr Gly Cys Asn Thr Glu His His Cys Ile Gly Gly Gly Tyr Phe  
 260 265 270  
 Pro Glu Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp  
 275 280 285  
 Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Glu Ile Thr  
 290 295 300  
 Glu Ala Ala Val Leu Leu Phe Tyr Arg  
 305 310  
 <210> 32  
 <211> 229  
 <212> PRT  
 <213> Homo sapiens  
 <400> 32  
 Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Leu Ala Ala  
 1 5 10 15  
 Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu  
 20 25 30  
 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe  
 35 40 45  
 Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val  
 50 55 60  
 Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

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65 70 75 80  
Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr  
85 90 95  
Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe  
100 105 110  
Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn  
115 120 125  
Met Gly Glu Gln Ala Gln Glu Asp Tyr Lys Lys Tyr Ile Thr  
130 135 140  
Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile  
145 150 155 160  
Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu  
165 170 175  
Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe  
180 185 190  
Asp Arg Val Asn Phe Thr Ser Met Val Asn Leu Val Val Met Val Val  
195 200 205  
Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys  
210 215 220  
Arg Lys Ser Arg Thr  
225  
<210> 33  
<211> 467  
<212> PRT  
<213> Homo sapiens  
<400> 33  
Met Arg Pro Gln Glu Leu Pro Arg Leu Ala Phe Pro Leu Leu Leu Leu  
1 5 10 15  
Leu Leu Leu Leu Leu Pro Pro Pro Cys Pro Ala His Ser Ala Thr  
20 25 30  
Arg Phe Asp Pro Thr Trp Glu Ser Leu Asp Ala Arg Gln Leu Pro Ala  
35 40 45  
Trp Phe Asp Gln Ala Lys Phe Gly Ile Phe Ile His Trp Gly Val Phe

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50 55 60  
Ser Val Pro Ser Phe Gly Ser Glu Trp Phe Trp Trp Tyr Trp Gln Lys  
65 70 75 80  
Glu Lys Ile Pro Lys Tyr Val Glu Phe Met Lys Asp Asn Tyr Pro Pro  
85 90 95  
Ser Phe Lys Tyr Glu Asp Phe Gly Pro Leu Phe Thr Ala Lys Phe Phe  
100 105 110  
Asn Ala Asn Gln Trp Ala Asp Ile Phe Gln Ala Ser Gly Ala Lys Tyr  
115 120 125  
Ile Val Leu Thr Ser Lys His His Glu Gly Phe Thr Leu Trp Gly Ser  
130 135 140  
Glu Tyr Ser Trp Asn Trp Asn Ala Ile Asp Glu Gly Pro Lys Arg Asp  
145 150 155 160  
Ile Val Lys Glu Leu Glu Val Ala Ile Arg Asn Arg Thr Asp Leu Arg  
165 170 175  
Phe Gly Leu Tyr Tyr Ser Leu Phe Glu Trp Phe His Pro Leu Phe Leu  
180 185 190  
Glu Asp Glu Ser Ser Ser Phe His Lys Arg Gln Phe Pro Val Ser Lys  
195 200 205  
Thr Leu Pro Glu Leu Tyr Glu Leu Val Asn Asn Tyr Gln Pro Glu Val  
210 215 220  
Leu Trp Ser Asp Gly Asp Gly Ala Pro Asp Gln Tyr Trp Asn Ser  
225 230 235 240  
Thr Gly Phe Leu Ala Trp Leu Tyr Asn Glu Ser Pro Val Arg Gly Thr  
245 250 255  
Val Val Thr Asn Asp Arg Trp Gly Ala Gly Ser Ile Cys Lys His Gly  
260 265 270  
Gly Phe Tyr Thr Cys Ser Asp Arg Tyr Asn Pro Gly His Leu Leu Pro  
275 280 285  
His Lys Trp Glu Asn Cys Met Thr Ile Asp Lys Leu Ser Trp Gly Tyr  
290 295 300  
Arg Arg Glu Ala Gly Ile Ser Asp Tyr Leu Thr Ile Glu Glu Leu Val  
305 310 315 320  
Lys Gln Leu Val Glu Thr Val Ser Cys Gly Gly Asn Leu Met Asn  
325 330 335

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Ile Gly Pro Thr Leu Asp Gly Thr Ile Ser Val Val Phe Glu Glu Arg  
340 345 350  
Leu Arg Glu Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr  
355 360 365  
5 Glu Thr His Thr Trp Arg Ser Glu Asn Asp Thr Val Thr Pro Asp Val  
370 375 380  
Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu  
385 390 395 400  
Lys Trp Pro Thr Ser Gly Glu Leu Phe Leu Gly His Pro Lys Ala Ile  
405 410 415  
10 Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Glu Pro Leu Asn  
420 425 430  
Trp Ile Ser Leu Glu Glu Asn Gly Ile Met Val Glu Leu Pro Glu Leu  
435 440 445  
15 Thr Ile His Glu Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr  
450 455 460  
Asn Val Ile  
465  
20 <210> 34  
<211> 99  
<212> PRT  
<213> Homo sapiens  
25 <400> 34  
Met Asp Asn Val Glu Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser  
1 5 10 15  
Val Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu  
20 25 30  
30 Val Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro  
35 40 45  
Glu Thr Thr Thr Leu Thr Val Gly Gly Val Val Phe Ala Leu Val Thr  
50 55 60  
Ala Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu  
65 70 75 80

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Phe Asn Pro Ser Gly Pro Tyr Glu Glu Lys Pro Val His Glu Lys Lys  
85 90 95  
Glu Val Leu  
5 <210> 35  
<211> 189  
<212> PRT  
<213> Homo sapiens  
10 <400> 35  
Met Glu Glu Gly Gly Asn Leu Gly Gly Leu Ile Lys Met Val His Leu  
1 5 10 15  
Leu Val Leu Ser Gly Ala Trp Gly Met Glu Met Trp Val Thr Phe Val  
20 25 30  
15 Ser Gly Phe Leu Leu Phe Arg Ser Leu Pro Arg His Thr Phe Gly Leu  
35 40 45  
Val Glu Ser Lys Leu Phe Pro Phe Tyr Phe His Ile Ser Met Gly Cys  
50 55 60  
Ala Phe Ile Asn Leu Cys Ile Leu Ala Ser Glu His Ala Trp Ala Glu  
65 70 75 80  
Leu Thr Phe Trp Glu Ala Ser Glu Leu Tyr Leu Leu Phe Leu Ser Leu  
85 90 95  
Thr Leu Ala Thr Val Asn Ala Arg Trp Leu Glu Pro Arg Thr Thr Ala  
100 105 110  
25 Ala Met Trp Ala Leu Glu Thr Val Glu Lys Glu Arg Gly Leu Gly Gly  
115 120 125  
Glu Val Pro Gly Ser His Glu Gly Pro Asp Pro Tyr Arg Glu Leu Arg  
130 135 140  
30 Glu Lys Asp Pro Lys Tyr Ser Ala Leu Arg Glu Asn Phe Phe Arg Tyr  
145 150 155 160  
His Gly Leu Ser Ser Leu Cys Asn Leu Gly Cys Val Leu Ser Asn Gly  
165 170 175  
Leu Cys Leu Ala Gly Leu Ala Leu Glu Ile Arg Ser Leu  
180 185

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<210> 36  
<211> 363  
<212> PRT  
<213> Homo sapiens

5

<400> 36  
Met Val Asp Ser Leu Leu Ala Val Thr Leu Ala Gly Asn Leu Gly Leu  
1 5 10 15  
Thr Phe Leu Arg Gly Ser Gln Thr Gln Ser His Pro Asp Leu Gly Thr  
20 25 30  
Glu Gly Cys Trp Asp Gln Leu Ser Ala Pro Arg Thr Phe Thr Leu Leu  
35 40 45  
Asp Pro Lys Ala Ser Leu Leu Thr Lys Ala Phe Leu Asn Gly Ala Leu  
50 55 60  
15 Asp Gly Val Ile Leu Gly Asp Tyr Leu Ser Arg Thr Pro Gln Pro Arg  
65 70 75 80  
Pro Ser Leu Ser His Leu Leu Ser Gln Tyr Tyr Gly Ala Gly Val Ala  
85 90 95  
Arg Asp Pro Gly Phe Arg Ser Asn Phe Arg Arg Gln Asn Gly Ala Ala  
100 105 110  
Leu Thr Ser Ala Ser Ile Leu Ala Gln Gln Val Trp Gly Thr Leu Val  
115 120 125  
Leu Leu Gln Arg Leu Glu Pro Val His Leu Gln Leu Cys Met Ser  
130 135 140  
25 Gln Glu Gln Leu Ala Gln Val Ala Ala Asn Ala Thr Lys Glu Phe Thr  
145 150 155 160  
Glu Ala Phe Leu Gly Cys Pro Ala Ile His Pro Arg Cys Arg Trp Gly  
165 170 175  
Ala Ala Pro Tyr Arg Gly Arg Pro Lys Leu Leu Gln Leu Pro Leu Gly  
180 185 190  
30 Phe Leu Tyr Val His His Thr Tyr Val Pro Ala Pro Pro Cys Thr Asp  
195 200 205  
Phe Thr Arg Cys Ala Ala Asn Met Arg Ser Met Gln Arg Tyr His Gln  
210 215 220  
35 Asp Thr Gln Gly Trp Gly Asp Ile Gly Tyr Ser Phe Val Val Gly Ser

225 230 235 240  
Asp Gly Tyr Val Tyr Glu Gly Arg Gly Trp His Trp Val Gly Ala His  
245 250 255  
Thr Leu Gly His Asn Ser Arg Gly Phe Gly Val Ala Ile Val Gly Asn  
260 265 270  
Tyr Thr Ala Ala Leu Pro Thr Glu Ala Ala Leu Arg Thr Val Arg Asp  
275 280 285  
Thr Leu Pro Ser Cys Ala Val Arg Ala Gly Leu Leu Arg Pro Asp Tyr  
290 295 300  
Ala Leu Leu Gly His Arg Gln Leu Val Arg Thr Asp Cys Pro Gly Asp  
305 310 315 320  
Ala Leu Phe Asp Leu Leu Arg Thr Trp Pro His Phe Thr Ala Thr Val  
325 330 335  
Lys Pro Arg Pro Ala Arg Ser Val Ser Lys Arg Ser Arg Arg Glu Pro  
340 345 350  
Pro Pro Arg Thr Leu Pro Ala Thr Asp Leu Gln  
355 360  
<210> 37  
<211> 249  
<212> PRT  
<213> Homo sapiens

20

<400> 37  
Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala Gly Leu Leu  
1 5 10 15  
Gly Ala Gly Ala Cys Tyr Cys Ile Tyr Arg Leu Thr Arg Gly Arg Arg  
20 25 30  
Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys Ser Ala Glu Asp  
35 40 45  
Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala Glu Gln Leu Gln  
50 55 60  
Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro Val Ile Ile Glu  
65 70 75 80  
Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Ala Phe Ser Val Asn Gln  
35

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85 90 95  
Ala Ile Ile Arg Glu Leu Gly Gly Ile Pro Ile Val Ala Asn Lys Ile  
100 105 110  
Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu Asn Ala Leu Asn  
5 115 120 125  
Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile Lys Val Gln Val  
130 135 140  
Leu Lys Leu Leu Leu Asn Leu Ser Glu Asn Pro Ala Met Thr Glu Gly  
145 150 155 160  
10 Leu Leu Arg Ala Gln Val Asp Ser Ser Phe Leu Ser Leu Tyr Asp Ser  
165 170 175  
His Val Ala Lys Glu Ile Leu Leu Arg Val Leu Thr Leu Phe Gln Asn  
180 185 190  
Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala Val Gln Pro Thr  
15 195 200 205  
Phe Thr Glu Gly Ser Leu Phe Leu Leu His Gly Glu Cys Ala  
210 215 220  
Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala Glu Val Lys Glu  
225 230 235 240  
20 Lys Val Val Thr Ile Ile Pro Lys Ile  
245  
<210> 38  
<211> 98  
<212> PPT  
25 <213> Homo sapiens  
<400> 38  
Met Ala Ser Leu Leu Cys Cys Gly Pro Lys Leu Ala Ala Cys Gly Ile  
30 1 5 10 15  
Val Leu Ser Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe  
20 25 30  
Phe Asn Val His Ser Ala Val Leu Ile Glu Asp Val Pro Phe Thr Glu  
35 35 40 45  
Lys Asp Phe Glu Asn Gly Pro Gln Asn Ile Tyr Asn Leu Tyr Glu Gln

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50 55 60  
Val Ser Tyr Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Gly  
65 70 75 80  
Gly Phe Ser Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met  
5 85 90 95  
Val Arg  
<210> 39  
<211> 172  
<212> PPT  
10 <213> Homo sapiens  
<400> 39  
Met Val Gly Pro Ala Pro Arg Arg Arg Leu Arg Pro Leu Ala Ala Leu  
15 1 5 10 15  
Ala Leu Val Leu Ala Leu Ala Pro Gly Leu Pro Thr Ala Arg Ala Gly  
20 25 30  
Gln Thr Pro Arg Pro Ala Glu Arg Gly Pro Pro Val Arg Leu Phe Thr  
35 40 45  
20 Glu Glu Glu Leu Ala Arg Tyr Gly Gly Glu Glu Glu Asp Gln Pro Ile  
50 55 60  
Tyr Leu Ala Val Lys Gly Val Val Phe Asp Val Thr Ser Gly Lys Glu  
65 70 75 80  
Phe Tyr Gly Arg Gly Ala Pro Tyr Asn Ala Leu Thr Gly Lys Asp Ser  
25 85 90 95  
Thr Arg Gly Val Ala Lys Met Ser Leu Asp Pro Ala Asp Leu Thr His  
100 105 110  
Asp Thr Thr Gly Leu Thr Ala Lys Glu Leu Glu Ala Leu Asp Glu Val  
30 115 120 125  
Phe Thr Lys Val Tyr Lys Ala Lys Tyr Pro Ile Val Gly Tyr Thr Ala  
130 135 140  
Arg Arg Ile Leu Asn Glu Asp Gly Ser Pro Asn Leu Asp Phe Lys Pro  
145 150 155 160  
Glu Asp Gln Pro His Phe Asp Ile Lys Asp Glu Phe  
35 165 170

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6 Met Met Pro Ser Arg Thr Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser Ser Lys 15  
 1 Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile Asp Leu 30  
 20 Gln Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile Ala Leu 45  
 35 Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile Gly Ser 60  
 50 Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg Ala Val 75  
 65 Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe Tyr His 90  
 85 Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr Ser Tyr 110  
 100 Asp Asp Ile Pro Asp Phe Asp Asp 120  
 115  
 25 <210> 41  
 <211> 939  
 <212> DNA  
 <213> Homo sapiens  
 30 <400> 41  
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 gaggttaata cttacttcaa ggaatggacc tgtttcttct cttccattct gccacagaac 120  
 tgcaggagaa tcaangacga atgtctagt gcaattgatg gcttgtatt tctccgact 180  
 gagaatggtg ttacttccca gaccttctgt gacatgacct ctgggggtgg cggctggacc 240  
 ctggtggcca gcgtgcatga gaatgaatg cgtgggaagt gcaaggatgg cgatcgtgg 300

360 tccagtcagc agggagcaga agagactac ccagaggggg ccggcaactg ggcacactac  
 420 aacactttg gatctgcaga gggggccacg agcatgact acagaaaccc tggctactac  
 480 gacatccagg ccaaggacct gggcatctgg cactgccc aaagtccc catgcagac  
 540 tggagaaca gctccctgct gaggtaacc ccggacactg gcttccca gacactggga  
 600 cataactgt ttggcatcta ccagaatat ccagtgaat atggagaag aaagtgtgg  
 660 actgaacg gcccggtgat cctgtggtc tatgatttg gcgacgcca gaaacagca  
 720 tctattact caccctatgg ccagcgggaa ttaactcgg gatttcta gtcagggtg  
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 840 actgagacc actgcattgg tggaggagga tacttccag aggcagctcc ccagcagtgt  
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 gactaccag ttltcgttg agcaggatta gatattgatt tccatcttgc ctctccaga 240  
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 gttgtgatt acatgttctg cttagcaat acattcaga ccatttctga gaagtgtatt 360  
 ttcttgaat taactcaga taatatgga gaacaggac aagaacaga agattggaaq 420  
 aaatatata ctggcacaga tatattgat atgaanctgg agcaactct ggaatccatc 480  
 aacagcata agtccagact angcaaaagt gggcacatac aaatttct tagagcattt 540  
 gaagctcgtg atogaacat acaagaagc aacttgata gactcaatt ctggtctatg 600  
 gttcaattag tggctatggt ggtggtgta gccattcaag ttatatgct gaagagtatg 660  
 30 ttggaagata agaggaaag tagaact 687  
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 <212> DNA  
 <213> Homo sapiens  
 35

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	ctggagagccc gcccagctgcgc cgcgtcgctt gaccagggcca agttcgacat cttaacccaa	180
	tggcgagctgt ttcccgctgcgc cagcttcggt agcgagctgtg tctgtgtgtta ttggcnaaaag	240
	gaaaagatacc cgaagctabgt ggaattatcg aaagataat accctccctag tttaaatat	300
	gaagattttg gaccacatit tacagcaaaa ttitttaatg ccacacagtg ggcagatatt	360
	tttcagggcct ctgttgcccaa ataatctgtc ttancttcca aaacatcatg agcttttacc	420
10	ttgttgggggt cagaatatttc gtcggaacttg aatgcacatg atggaggggc caagggggagc	480
	attgtcaagtg aacttgaggt agccattatg aacagaaatg accctcgctt tggactgtcac	540
	tattcccttt ttgaatgtgt tcatccgctc ttccctggag atgaatccag ttcatcccat	600
	aagcggcaat ttccagtttc taagacatg ccagagctct atgagttagt gaaacaatat	660
	cagcctgagtg ttctgtgtgc ggaatgtgac ggaaggagac cggatcaata ctggaaacagc	720
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	gactgtctgg gaggctgtgag catctgtatg catgtgtggt tctataccct cagtgtacgt	840
	tataaccag gacatcttt gccaatataa tgggnaaact gcatgacaaat agaaanaatg	900
	tctgtgggtc ataggagggg agcttgaatc tctgactatc ttacaatga agaatgtgtg	960
20	aaagaaattg taagagacagt ttcatgtgga ggaahcttt ttatgaatat tgggcacaca	1020
	ctagatggca ccaattctgt agttttgag gaggagatga ggaatgggg gtccctggcta	1080
	aaagtaatg gagaagctat ttatgaacc catnactggc gatcccaaga tgaactgttc	1140
	accceagatg tgtgttacaac atccagagct aaagaaatat taagtatgc catltttct	1200
	aaatggccca catcagggca gctgttcctt ggcacatcca aaagtattct gggggcaaca	1260
	gagctgaaac taactgggca tggaaagcca cttaactgga ttctcttga gcaaaatggc	1320
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	ctagccctga cttaatgtgt c	1401
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	<400> 44	
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	gtgaagatgc tggcgttga tattatcaac tcaactgtaa caacagatatt catgtcatc	120

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	gtatctgtgt tgcgaactgat accagaaacc aaacatitga caattgtgtg aggggtgttt	180
	gaaattitga cagagtatag ctgtcttgcg gacggggccc ttatttaccg gaacttctcg	240
	ttcaatccca ggggtacctta ccagaaaag ccgtgtcatg aaaaaaaga agttttg	297
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6	<211> 567	
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	cttcccagac ataaccttgg actatgtcag agcaaacctc tccccttcta ctccaacac	180
	tcaatgggtc gttgcttcat caaaccttgc atcttggctt caaagcatgc ttgggtcag	240
	ctcaaatct gggagggccag ccagctttac ctgtcttccc tgaagctaac gctggccact	300
15	gtcaagccc gctgtcttga accccgagac aaagcttcca tgttggccct gcaaacctg	360
	ggaaagagag gagggtctgg tggggagtta ccaggagagc accaggttcc cgaatccatc	420
	cgcagactgc gagaagagga ccccaagtac agtgcctccc gccagaaatt ctccgctac	480
	catyggctgc cctctcttgg caatctgggc tggctcttga gaaatgggtc ctgtctgct	540
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30	ggcccttga cctttacgt ttggacccc aaggaatcc tpttaaccaa ggccttccctc	180
	aatgggccc tgaatgtgtt catcttggg gaactactga gccggagctcc tgaaccccg	240
	ccatccctca gcaacttgc gaccagtaac tatggggctg ggttggccag agaccaggg	300
	ttccgcaaga acttccagcg gcaaaaggt gctgtcttga cttaagcttc catcttggcc	360
	cagagaggtt ggggaacctc tptcttcta cagaagcttg agcagtaaca cctcaagctt	420
35	caatgtatga gcaagaaca gcttggccag gttgcttcca atgtatacaa ggaattacat	480

45/177

46/177

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gtgctgtcac caccctgacc ggaactacg cgtgcgcag ccaactgcy ctccatgag 660  
cgtacacacc agaacacgaa aggtctgggga gaactcggt acagtttgtt ggtggctcg 720  
gacggtacag tgcacgaggg acgcgcttgg caetgggtgg gacccacac gctcgccac 780  
aactcccggg gcttgggtgt ggcacatgtg ggaactaca ccgcyggcgt gccacacgag 840  
gcccctctgc gacgggtgc gacacgctc ccgagttgtg cgggtgcgcg cggcctctcg 900  
cggcgagact acgctgtgt cactgcacgc cagctggtgc gacccgactg ccccgcgac 960  
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gacctccaa 1089

&lt;210&gt; 47

&lt;211&gt; 747

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 47

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cgtctctcga agtccgcaga agacttaact gatgggttcat atgatgatgt tctaatgct 180  
gaacacctic agaacctct ttacctgctg gaggcaacgg aggtacctgt aattattgaa 240  
aagctttga ttactttggg taacaaatgca gctttttcag ttacccaagc tattattcgt 300  
gaattgggtg gtattccaat tgttgaac aaaaataccc attccaacca gagtattaaa 360  
gagaaggttt taatgcaact aaataacctg agtgtgaatg ttgaanaatca aatcaagata 420  
aaggtgcaag ttgtgaact gcttttgaat ttgtctgaaa atcccgccat gacagaggga 480  
cttctccgtg cccaagtggg ttacatctc ctttcccttt atgacggcca cgtagcaaaag 540  
gagatcttc ttcgagtact taccgtatit cagaaataaa agaaactgct caaaatagaa 600  
ggccatttag ctgtgcagcc tacttcaact gaaggttcat tgttttctct gttacatgga 660  
gaagaatgtg ccagaaat agaggttita gtgtacacc atgatgcaga ggtgaaggaa 720  
aaggttgtaa caataatcc caaatc 747

&lt;210&gt; 48

&lt;211&gt; 294

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 48

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tggggagfga tcatgttgat aatgctcga atattttca atgtccatc cgtgtgttg 120  
attgagcag ttcccttcc ggcgaagat ttgagaatg gcccacgaa catataaac 180  
cttaccagc aagtacgcta caactgttc atcgtgcag gctttacct cctctcaga 240  
ggttctatt tctgcaagt tggctcaat aagcgaagg aatacatggt gcgc 294

10 &lt;210&gt; 49

&lt;211&gt; 516

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

16 &lt;400&gt; 49

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gcgtggccc cggggctgcc caccgcgg gcggggcaga caccgcgcc tgcgagcgg 120  
gggcccacg tgcgctttt caccggagg gagctggccc gctatggcg ggaaggaggaa 180  
gacagccca tctactggc agtgaaggga gtgggtgttg atgtcacctc cggaaaggag 240  
ttttatgac gaggagccc ctacaatgcc ttgacgggga aggaactcac tagaggggta 300  
gccaagatgt cctggatcc tgcagacctc accaatgaca ctacgggtct caccggcaag 360  
gaactgggg cctggatga ggtcttacc aagtgtaaa aagcacaata ccccatctc 420  
ggctacatg ccggagaaat tctcaatgag gatggcagcc ctcaacttggg ctteagacct 480  
gaagaccag cccattttga catcaaggat gagtgc 516

26 &lt;210&gt; 50

&lt;211&gt; 360

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

30 &lt;400&gt; 50

atgatgcct cccgtaccca cctggctact ggaatccca gtagtaagt gaatatctca 60  
aggcttcca gacagacga tggctacatt gacctcagt ttaagaaac cctctctag 120  
atccctata aggcacgcg acttgcaact gtgtgtttt tgattggcg cttctctatt 180  
attatagct cctctctgt gtcaggctac atcagcaag gggggcgaga ccggcgctt 240



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ccagtgctga tcaatggat tctgtgttc ctaccggat ttaccacct ggcgctgc 300  
 tactatgat ccaagagcta ccgtgtgtac tccatgatg acattccaga cttgatgac 360

<210> 51  
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 <212> DNA  
 <213> Homo sapiens  
 <220>  
 <221> CDS  
 <222> (2)...(943)

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 Met Asn Gln Leu Ser Phe Leu Leu Phe Leu Ile Ala Thr Thr Arg Gly  
 1 5 10 15  
 tgg agt aca gat gag gct aat act tac ttc aag gaa tgg acc tgt tct 97  
 Trp Ser Thr Asp Gln Ala Asn Thr Tyr Phe Lys Gln Trp Thr Cys Ser  
 20 25 30  
 tgg tct cca tct ctg ccc aga agc tgc aag gaa atc aaa gaa gaa tgt 145  
 Ser Ser Pro Ser Leu Pro Arg Ser Cys Lys Gln Ile Lys Asp Gln Cys  
 35 40 45  
 cct agt gca ttt gat ggc ctg tat ttt ctg cgc act gag aat ggt gtt 193  
 Pro Ser Ala Phe Asp Gly Leu Tyr Phe Leu Arg Thr Gln Asn Gly Val  
 50 55 60  
 atc tac cag acc ttc tgt gac atg acc tct ggg ggt ggc ggc tgg acc 241  
 Ile Tyr Gln Thr Phe Cys Asp Met Thr Ser Gly Gly Gly Trp Thr  
 65 70 75 80  
 ctg gtg ggc ago gtg cat gag aat gac atg cgt ggg aag tgc aag gtg 289  
 Leu Val Ala Ser Val His Gln Asn Asp Met Arg Gly Lys Cys Thr Val  
 85 90 95  
 ggc gat cgc tgg tcc agt cag cag ggc agc aaa gca gac tac cca gag 317  
 Gly Asp Arg Trp Ser Ser Gln Gln Gly Ser Lys Ala Asp Tyr Pro Gln  
 100 105 110  
 ggg gac ggc aac tgg gcc aac tac aac acc ttt gga tct gca gag gcg 385  
 Gly Asp Gly Asn Trp Ala Asn Tyr Asn Thr Phe Gly Ser Ala Gln Ala

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115 120 125  
 gcc aag agc gat gac tac aag aac cct ggc tac tac gac atc cag gcc 433  
 Ala Thr Ser Asp Asp Tyr Lys Asn Pro Gly Tyr Tyr Asp Ile Gln Ala  
 130 135 140  
 aag gac ctg ggc atc tgg cgc gtg ccc aat aag tcc ccc atg cag cac 481  
 Lys Asp Leu Gly Ile Trp His Val Pro Asn Lys Ser Pro Met Gln His  
 145 150 155 160  
 tgg aga aac agc tcc ctg ctg agg tac cgc aag gac act ggc ttc ctg 529  
 Trp Arg Asn Ser Ser Leu Leu Arg Tyr Arg Thr Asp Thr Gly Phe Leu  
 165 170 175  
 cag aca ctg gga cat aat ctg ttt ggc atc tac cag aaa tat cca gtg 577  
 Gln Thr Leu Gly His Asn Leu Phe Phe Ile Tyr Gln Lys Tyr Pro Val  
 180 185 190  
 aaa tac gga gaa gga aag tgt tgg act gac aac ggc ccg gtg atc cct 625  
 Lys Tyr Gly Gln Gly Lys Cys Trp Thr Asp Asn Gly Pro Val Ile Pro  
 195 200 205  
 gtg gtc tat gat ttt ggc gac gcc cag aaa aca gaa tct tat tac tca 673  
 Val Val Tyr Asp Phe Gly Asp Ala Gln Lys Thr Ala Ser Tyr Tyr Ser  
 210 215 220  
 ccc tat ggc cag cgg gaa ttc act gcg gga ttt gtt cag ttc aag gta 721  
 Pro Tyr Gly Gln Arg Gln Phe Thr Ala Gly Phe Val Gln Phe Arg Val  
 225 230 235 240  
 ttt aat aac gag aga gca gcc aac gcc ttg tgt gct gga atg aag gtc 769  
 Phe Asn Asn Gln Arg Ala Ala Asn Ala Leu Cys Ala Gly Met Arg Val  
 245 250 255  
 acc gga tgt aac aac gag cac cac tgc att ggt gga gga gaa ttt 817  
 Thr Gly Cys Asn Thr Gln His His Cys Ile Gly Gly Gly Tyr Phe  
 260 265 270  
 cca gag ggc agt ccc cag cag tgc gga gat ttt tct ggt ttt gat tgg 865  
 Pro Gln Ala Ser Pro Gln Gln Cys Gly Asp Phe Ser Gly Phe Asp Trp  
 275 280 285  
 agt gga tat gga act cat gtt ggt tac agc agc agc cgt gag ata act 913  
 Ser Gly Tyr Gly Thr His Val Gly Tyr Ser Ser Ser Arg Gln Ile Thr  
 290 295 300  
 gag gca gct gtg ctt cta ttc tct cgt tgaaggttt gtggagggga 960

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Glu Ala Ala Val Leu Leu Phe Tyr Arg

305 310

accagaccc ctctctccaa ccatgagatc ccaaggatgg agaaacactt acccagtagc 1020

tagaatgta atggcgag agaaacact aaatcatatt gactc 1065

6

&lt;210&gt; 52

&lt;211&gt; 937

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

10 &lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (177)...(866)

&lt;400&gt; 52

15 cttttggaga actgagcttc tctttggag ggaagtgtcg cgcgcgcgc ggcgcgcacc 60

tggagttctc tcaagactcca gatttccctg tcaaccaga ggaagtccaga gaggaanagc 120

ggagcggaga caacagtaacc tgacgcctat ttaagcccg gacgcacca gcaggg 176

atg ggc gac aag atc tgg ctg ccc ttc ccc gtg etc ctt ctg gcc get 224

Met Gly Asp Lys Ile Trp Leu Pro Phe Pro Val Leu Leu Ala Ala

20 1 5 10 15

ctg cct ccg gtg ctg cct ggg gcg gcc ggc ttc aca cct tcc etc 272

Leu Pro Pro Val Leu Leu Pro Gly Ala Ala Gly Phe Thr Pro Ser Leu

20 25 30

gat agc gac ttc acc ttt acc ctt gcc gcc gcc agc gag tgc ttc 320

25 Asp Ser Asp Phe Thr Phe Thr Leu Pro Ala Gly Gln Lys Glu Cys Phe

35 40 45

tac aag ccc atg ccc ctg aag gcc teg ctg gag atc gag tac caa gtt 368

Tyr Gln Pro Met Pro Leu Lys Ala Ser Leu Glu Ile Glu Tyr Gln Val

50 55 60

30 tta gat gga gca gga tta gat att gat ttc cat ctt gcc tct cca gaa 416

Leu Asp Gly Ala Gly Leu Asp Ile Asp Phe His Leu Ala Ser Pro Glu

65 70 75 80

ggc aaa acc tta gtt ttt gaa caa aga aaa tca gat gga gtt cac act

Gly Lys Thr Leu Val Phe Glu Gln Arg Lys Ser Asp Gly Val His Thr

85 90 95

35

gta gag act gaa gtt ggt gat tac atg ttc tgc ttt gac aat aca ttc 512

Val Glu Thr Glu Val Gly Asp Tyr Met Phe Cys Phe Asp Asn Thr Phe

100 105 110

agc ecc att tct gag aag gtg att ttc ttt gaa tta atc ctg'gat aat 560

Ser Thr Ile Ser Glu Lys Val Ile Phe Phe Glu Leu Ile Leu Asp Asn

115 120 125

atg gga gaa cag gca caa gaa gat tgg aag aaa tat att act 608

Met Gly Glu Gln Ala Gln Glu Asp Trp Lys Lys Tyr Ile Thr

130 135 140

10 ggc eca gat ata ttg gat atg aaa ctg gaa'gac atc ctg gaa tcc atc 656

Gly Thr Asp Ile Leu Asp Met Lys Leu Glu Asp Ile Leu Glu Ser Ile

145 150 155 160

aac agc atc aag tcc aga cta agc aaa agt ggg cac ata caa att ctg 704

Asn Ser Ile Lys Ser Arg Leu Ser Lys Ser Gly His Ile Gln Ile Leu

165 170 175

15 ctt aga gaa ttt gaa get cgt gat cga aac ata caa gaa agc aac ttt 752

Leu Arg Ala Phe Glu Ala Arg Asp Arg Asn Ile Gln Glu Ser Asn Phe

180 185 190

20 gat aga gtc aat ttc tgg tct atg gtt aat tta gtg gtc atg gtg gtg 800

Asp Arg Val Asn Phe Trp Ser Met Val Asn Leu Val Val Met Val Val

195 200 205

gtg tca gcc att caa gtt tat atg ctg aag agt ctg ttt gaa gat aag 848

Val Ser Ala Ile Gln Val Tyr Met Leu Lys Ser Leu Phe Glu Asp Lys

210 215 220

25 agg aaa agt aga act taaaactcca aactagagta cgtcaacattg aaaaatg 900

Arg Lys Ser Arg Thr

225

aggcataaaa atgcataaaa ctgttacagt cangacc 937

30 &lt;210&gt; 53

&lt;211&gt; 1678

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

35 &lt;221&gt; CDS



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ctg agg caa atg ggg tcc tgg cta aaa gtc aat gga gaa gct att tat 1159  
Leu Arg Gln Met Gly Ser Trp Leu Lys Val Asn Gly Glu Ala Ile Tyr 365  
355  
gaa acc cat acc tgg cga tcc cag aat gac act gtc acc cca gat gtg 1207  
Glu Thr His Thr Trp Arg Ser Gln Asn Asp Thr Val Thr Pro Asp Val 360  
370 375 380  
tgg tac aca tcc aag cct aaa gaa aaa tta gtc tat gcc att ttt ott 1255  
Trp Tyr Thr Ser Lys Pro Lys Glu Lys Leu Val Tyr Ala Ile Phe Leu 395  
385 390 395 400  
aaa tgg ccc aca tca gga cag ctg ttc ctt ggc cat ccc aaa gct att 1303  
Lys Trp Pro Thr Ser Gly Gln Leu Phe Leu Gly His Pro Lys Ala Ile 405  
400 410 415  
ctg ggg gca aca gag gtg aaa cta ctg ggc cat gga cag cca ctt aac 1351  
Leu Gly Ala Thr Glu Val Lys Leu Leu Gly His Gly Gln Pro Leu Asn 420  
425 430  
tgg att tct ttg gag caa aat ggc att atg gta gaa ctg cca cag cta 1399  
Trp Ile Ser Leu Glu Gln Asn Gly Ile Met Val Glu Leu Pro Gln Leu 435  
440 445  
acc att cat cag atg ccg tgt aaa tgg ggc tgg gct cta gcc ctg act 1447  
Thr Ile His Gln Met Pro Cys Lys Trp Gly Trp Ala Leu Ala Leu Thr 450  
455 460  
aat gtg atc taaagtgcag cagagtggct gatgtgcaa gttatgcta aggc 1500  
Asn Val Ile 465  
taggaactat caggtgtcta taattgagc acatggagaa agcaaatgta aaactggata 1560  
agaaattat ttggcagtt cagcccttcc ccttttccc actaaatttt tcttaaat 1620  
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<212> DNA  
<213> Homo sapiens  
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cagccagctg agaagagttg agggaaagtg ctgctgctgg gtctgcagac ggg atg 116  
Met  
gat aac gtg cag ccg aaa ata aaa cat cgc ccc ttc tgc ttc agt gtg 164  
Asp Asn Val Gln Pro Lys Ile Lys His Arg Pro Phe Cys Phe Ser Val  
5 10 15  
aaa ggc cac gtg aag atg ctg cgg ctg gat att atc aac tca ctg gta 212  
Lys Gly His Val Lys Met Leu Arg Leu Asp Ile Ile Asn Ser Leu Val  
20 25 30  
aca aca gta ttc atg etc atc gta tct gtg ttg gca ctg ata cca gaa 260  
Thr Thr Val Phe Met Leu Ile Val Ser Val Leu Ala Leu Ile Pro Glu  
35 40 45  
acc aca aca ttg aca gtt ggt gga ggg gtg ttt gca ctt gtg aca gca 308  
Thr Thr Thr Leu Thr Val Gly Gly Val Phe Ala Leu Val Thr Ala  
50 55 60  
gta tgc tgt ctt gcc gac ggg gcc ctt att tac cgg aag ctt ctg ttc 356  
Val Cys Cys Leu Ala Asp Gly Ala Leu Ile Tyr Arg Lys Leu Leu Phe  
70 75 80  
aat ccc agc ggt cct tac cag caa aag cct gtg cat gaa aaa aaa gaa 404  
Asn Pro Ser Gly Pro Tyr Gln Gln Lys Pro Val His Glu Lys Lys Glu  
85 90 95  
gtt ttg taattttata ttacttttta gtttgatact aagtattaaa 450  
Val Leu  
catattctcg tattctt 467

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<211> 875  
<212> DNA  
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<220>  
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&lt;222&gt; (272)...(841)

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 Gly Gly Leu Ile Lys Met Val His Leu Leu Val Leu Ser Gly Ala Trp  
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 Gly Met Glu Met Trp Val Thr Phe Val Ser Gly Phe Leu Leu Phe Arg  
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 Ser Leu Pro Arg His Thr Phe Gly Leu Val Glu Ser Lys Leu Phe Pro  
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 Phe Tyr Phe His Ile Ser Met Gly Cys Ala Phe Ile Asn Leu Cys Ile  
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 Glu Leu Tyr Leu Leu Phe Leu Ser Leu Thr Leu Ala Thr Val Asn Ala  
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 cgc tgg ctg gaa ccc cgc acc aca gct gcc atg tgg gcc ctg caa acc  
 Arg Trp Leu Glu Pro Arg Thr Thr Ala Ala Met Trp Ala Leu Glu Thr  
 105 110 115  
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 Val Glu Lys Glu Arg Gly Leu Gly Gly Glu Val Pro Gly Ser His Glu  
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 ggt ccc gat ccc tac cgc cag ctg cga gag aag gac ccc aag tac agt  
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 cagatgccaa agccaagctcc ccaccgacc atg gtc gag agc ctc ctg gca gtc  
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 10 15 20  
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 Glu Ser His Pro Asp Leu Gly Thr Glu Gly Cys Trp Asp Glu Leu Ser  
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 ggc cct cgg acc ttc agc ctt ttg gac ccc aag gca tct ctg tta acc  
 Ala Pro Arg Thr Phe Thr Leu Leu Asp Pro Lys Ala Ser Leu Leu Thr  
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aag gcc ttc ctc aat ggc gcc ctg gat ggg gtc atc ctt gga gac tac 365  
 Lys Ala Phe Leu Asn Gly Ala Leu Asp Gly Val Ile Leu Gly Asp Tyr 70  
 60 65  
 ctg agc egg act cct gag ccc cgg cca tcc ctc agc cac ttg ctg agc 413  
 Leu Ser Arg Thr Pro Glu Pro Arg Pro Ser Leu Ser His Leu Leu Ser 85  
 75 80  
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 Gln Tyr Tyr Gly Ala Gly Val Ala Arg Asp Pro Gly Phe Arg Ser Asn 100  
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 Phe Arg Arg Gln Asn Gly Ala Ala Leu Thr Ser Ala Ser Ile Leu Ala 115  
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 Gln Gln Val Trp Gly Thr Leu Val Leu Leu Gln Arg Leu Glu Pro Val 135  
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 His Leu Gln Leu Gln Cys Met Ser Gln Gln Gln Leu Ala Gln Val Ala 150  
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 Ala Asn Ala Thr Lys Glu Phe Thr Glu Ala Phe Leu Gly Cys Pro Ala 165  
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 Ile His Pro Arg Cys Arg Trp Gly Ala Ala Pro Tyr Arg Gly Arg Pro 180  
 170 175  
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 Lys Leu Leu Gln Leu Pro Leu Gly Phe Leu Tyr Val His His Thr Tyr 195  
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 Val Pro Ala Pro Pro Cys Thr Asp Phe Thr Arg Cys Ala Ala Asn Met 210  
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 cgc tcc atg cag cgc tac cac cag gac acg caa ggc tgg gga gac atc 845  
 Arg Ser Met Gln Arg Tyr His Gln Asp Thr Gln Gly Trp Gly Asp Ile 225  
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 Gly Tyr Ser Phe Val Val Gly Ser Asp Gly Tyr Val Tyr Glu Gly Arg

235 240 245  
 ggc tgg cac tgg gtc ggc gcc cac acg ctc ggc cac aac tcc cgg ggc 941  
 Gly Trp His Trp Val Gly Ala His Thr Leu Gly His Asn Ser Arg Gly 250 255 260  
 5 ttc ggc gtc gcc ata gtc ggc aac tac acc ggc ggc ctg ccc acc gag 999  
 Phe Gly Val Ala Ile Val Gly Asn Tyr Thr Ala Ala Leu Pro Thr Glu 265 270 275 280  
 gcc gct ctg cgc acg gtc ggc gac acg ctc cgc agt tgc ggc gtc cgc 1037  
 Ala Ala Leu Arg Thr Val Arg Asp Thr Leu Pro Ser Cys Ala Val Arg 285 290 295  
 10 gcc ggc ctc ctg cgg cca gac tac ggc ctg ctg ggc cac cgc cag ctg 1085  
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 Val Arg Thr Asp Cys Pro Gly Asp Ala Leu Phe Asp Leu Leu Arg Thr 315 320 325  
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Met Gly Gly Pro Arg Gly Ala Gly Trp Val Ala Ala  
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Gly Leu Leu Leu Gly Ala Gly Tyr Cys Ile Tyr Arg Leu Thr  
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Arg Gly Arg Arg Gly Asp Arg Glu Leu Gly Ile Arg Ser Ser Lys  
30 35 40  
tcc gaa gaa gac tta act gat gat tca tca tat gat gat cta aat gct 314  
Ser Ala Glu Asp Leu Thr Asp Gly Ser Tyr Asp Asp Val Leu Asn Ala  
45 50 55 60  
gaa caa ctt cag aaa ctc ctt tac ctg ctg gag tca acg gag gat cct 362  
Glu Gln Leu Gln Lys Leu Leu Tyr Leu Leu Glu Ser Thr Glu Asp Pro  
65 70 75  
gta att att gaa aga gct ttg att act ttg ggt aac aat gca gcc ttt 410  
Val Ile Ile Glu Arg Ala Leu Ile Thr Leu Gly Asn Asn Ala Phe  
80 85 90  
tca gtt aac caa gct att att cgt gaa ttg ggt ggt att cca att gtt 458  
Ser Val Asn Gln Ala Ile Ile Arg Glu Leu Gly Ile Pro Ile Val  
95 100 105  
gca aac aaa atc aac cat tcc aac cag agt att aaa gag aaa gct tta 506  
Ala Asn Lys Ile Asn His Ser Asn Gln Ser Ile Lys Glu Lys Ala Leu  
110 115 120  
aat gca cta aat aac ctg agt gtc aat gtt gaa aat caa atc aag ata 554  
Asn Ala Leu Asn Asn Leu Ser Val Asn Val Glu Asn Gln Ile Lys Ile  
125 130 135 140  
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Lys Val Gln Val Leu Lys Leu Leu Asn Leu Ser Glu Asn Pro Ala  
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175 180 185  
cta ttt cag aat ata aag aac tgc ctg ctc aaa ata gaa ggc cat tta gct 746  
Leu Phe Gln Asn Ile Lys Asn Cys Leu Lys Ile Glu Gly His Leu Ala  
190 195 200  
gtg aag cct act ttc act gaa ggt tca ttg ttt ttc ctg tta cat gga 794  
Val Gln Pro Thr Phe Thr Glu Gly Ser Leu Phe Leu Leu His Gly  
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Glu Glu Cys Ala Gln Lys Ile Arg Ala Leu Val Asp His His Asp Ala  
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Ala Trp Gly Val Ile Met Leu Ile Met Leu Gly Ile Phe Phe Asn Val  
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40 45 50  
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Asn Cys Phe Ile Ala Ala Gly Leu Tyr Leu Leu Leu Gly Gly Phe Ser  
70 75 80  
ttc tgc caa gtt cgg etc aat aag cgc aag gaa tac atg gtg cgc 341  
Phe Cys Gln Val Arg Leu Asn Lys Arg Lys Glu Tyr Met Val Arg  
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Leu Arg Pro Leu Ala Ala Leu Ala Leu Val Leu Leu Ala Leu Ala Pro Gly  
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Leu Pro Thr Ala Arg Ala Gly Gln Thr Pro Arg Pro Ala Glu Arg Gly  
30 35 40  
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Pro Pro Val Arg Leu Phe Thr Glu Glu Leu Ala Arg Tyr Gly Gly 55  
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Glu Glu Glu Asp Gln Pro Ile Tyr Leu Ala Val Lys Gly Val Val Phe  
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Asp Val Thr Ser Gly Lys Asp Phe Tyr Gly Arg Gly Ala Pro Tyr Asn  
75 80 85  
gcc ttg acg ggg aag gac tcc act aga ggg gta gcc aag atg tcc ttg 339  
Ala Leu Thr Gly Lys Asp Ser Thr Arg Gly Val Ala Lys Met Ser Leu  
90 95 100 105  
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Asp Pro Ala Asp Leu Thr His Asp Thr Thr Gly Leu Thr Ala Lys Glu  
110 115 120  
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Leu Glu Ala Leu Asp Glu Val Phe Thr Lys Val Tyr Lys Ala Lys Tyr  
125 130 135  
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Pro Ile Val Gly Tyr Thr Ala Arg Arg Ile Leu Asn Glu Asp Gly Ser  
140 145 150  
cct aac ctg gcc ttc aag cct gaa gac cag ccc cat ttt gac atc aag 531  
Pro Asn Leu Asp Phe Lys Pro Glu Asp Gln Pro His Phe Asp Ile Lys  
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Asp Glu Phe  
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Met Met Pro Ser Arg Thr Asn Leu Ala Thr Gly Ile Pro Ser

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agt aaa gtg aaa tat tca agt ctc tcc agc aca gac gat ggc tac att 216

Ser Lys Val Lys Tyr Ser Arg Leu Ser Ser Thr Asp Asp Gly Tyr Ile

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gac ctt cag ttt aag aaa acc cct cct aag atc cct tat aag gac atc 264

Asp Leu Glu Phe Lys Lys Thr Pro Pro Lys Ile Pro Tyr Lys Ala Ile

35 40 45

gca ctt ggc act gtg ctt ttt ttg att ggc ggc ttt cta att att ata 312

Ala Leu Ala Thr Val Leu Phe Leu Ile Gly Ala Phe Leu Ile Ile Ile

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Gly Ser Leu Leu Leu Ser Gly Tyr Ile Ser Lys Gly Gly Ala Asp Arg

65 70 75

ggc gtt cca gtg ctt atc att ggc att ctt gtg ttc cta ccc gga ttt 408

Ala Val Pro Val Leu Ile Ile Gly Ile Leu Val Phe Leu Pro Gly Phe

80 85 90

tac cac ctt cgc atc gct tac tcc gca tcc aaa ggc tac cgt ggt tac 456

Tyr His Leu Arg Ile Ala Tyr Tyr Ala Ser Lys Gly Tyr Arg Gly Tyr

95 100 105 110

tcc tat gat gac att cca gac ttt gat gac tagaaccac ccca 500

Ser Tyr Asp Asp Ile Pro Asp Phe Asp Asp

115 120

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gctggagact aagaattct gaacttga gatgtttaa aaaaatagc caagatttt 620

tggtgccttc ccaaatgtt taagtgaac taacttagc taattagac aagctcatt 680

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taaatagct taactgcnaa ttgttctgt tagaatagt aacatgtgt tatgtcaat 860

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ttctgcagat tattcctta accgcggac ttittgttgt ttcccttaga aacatgtagt 1220

ggtattatt taagtttat agcgtatgt ctgaacctt gttagatgac atcaattctg 1280

taagtattcc aagatcagc ctgatgact agaggaatag atcaacttag tttagtcta 1340

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Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Glu Leu Pro

35 40 45

Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe Ile Ser

50 55 60

Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr Pro Asn

65 70 75 80

Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Glu Lys Glu Phe Ile Thr

85 90 95

Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr Cys Phe

100 105 110

Ile Glu Phe Asp Asn Phe Ile Glu Arg Thr Lys Glu Arg Tyr Asn Asn

115 120 125

Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Glu Thr Glu

130 135 140

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Ile Lys Leu Arg Pro Tyr Gln Ile Ser Met Cys Glu Leu Gly Ser  
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 Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly Ala Gly  
 165 170 175  
 5 Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu Ser Gly  
 180 185 190  
 Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn Leu Ile  
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 Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly Asp Asp  
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 15 Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu Tyr Glu  
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 Thr Glu His Ser Ser Met Pro Val Glu Lys Asn Ile Thr Leu Glu Arg  
 65 70 75 80  
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 Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr Ser Cys Phe Phe  
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 Arg Gln Gln Lys Gln Gln Arg Gly Thr Phe Asn Phe Lys Val Pro Gln  
 145 150 155 160  
 10 Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val Gly Asp Ser Thr  
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 Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu Asn Trp Thr Trp  
 180 185 190  
 15 Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly Val Gln Met Asn  
 195 200 205  
 Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Gln Thr Lys Leu Lys Ile  
 210 215 220  
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 225 230 235 240  
 20 Phe Gln Leu Gly Gln Ser Gln Gln His Ile Gln Leu Val Leu Ser  
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 25 Leu Leu Val Ala Thr Ile Leu Leu Cys Gln Lys Tyr Thr Gln Lys Lys  
 275 280 285  
 Lys Lys His Ser Asp Gln Gly Lys Gln Phe Gln Gln Ile Gln Gln Leu  
 290 295 300  
 Lys Ser Asp Asp Ser Asn Gly Ile Gln Asn Asn Val Pro Arg His Arg  
 305 310 315 320  
 30 Lys Asn Gln Ser Leu Gly Gln  
 325

&lt;210&gt; 64

&lt;211&gt; 223

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<212> PRT  
 <213> Homo sapiens  
 <400> 64  
 5 Met Lys Phe Val Pro Cys Leu Leu Leu Val Thr Leu Ser Cys Leu Gly  
 1 5 10 15  
 Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Gly Gln Gln  
 20 25 30  
 Phe His Phe Gln Thr Gly Gly Arg Asp Ser Cys Thr Met Arg Pro Ser  
 35 40 45  
 10 Ser Leu Gly Gln Gly Ala Gly Gln Val Trp Leu Arg Val Asp Cys Arg  
 50 55 60  
 Asn Thr Asp Gln Thr Tyr Trp Cys Gln Tyr Arg Gly Gln Pro Ser Met  
 65 70 75 80  
 15 Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala Leu  
 85 90 95  
 Gln Gln Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val Leu  
 100 105 110  
 Arg Pro Ser Val Cys Arg Gln Ala Gly Pro Gln Ala His Met Gln Gln  
 115 120 125  
 20 Val Thr Ser Ser Leu Lys Gly Ser Pro Gln Pro Asn Gln Gln Pro Gln  
 130 135 140  
 Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr Gln  
 145 150 155 160  
 25 Ala Thr Gln Leu Gly Lys Asp Ser Met Gln Gln Leu Gly Lys Ala Lys  
 165 170 175  
 Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg Pro  
 180 185 190  
 Gly Gly Asn Gln Gln Ala Lys Lys Lys Ala Trp Gln His Cys Trp Lys  
 195 200 205  
 30 Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Phe Arg Gly  
 210 215 220

&lt;210&gt; 65

&lt;211&gt; 48

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70/177

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

&lt;400&gt; 65

5 Met Arg Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg

1

5

10

15

Ser Glu Ala Ser Ala Asn Leu Gly Val Pro Ser Lys Arg Leu Lys

20

25

30

Met Gln Tyr Ala Thr Gly Pro Leu Lys Phe Gln Ile Cys Val Ser

35

40

45

&lt;210&gt; 66

&lt;211&gt; 371

&lt;212&gt; PRT

15 &lt;213&gt; Homo sapiens

&lt;400&gt; 66

Met Ala Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val

1

5

10

15

20 Thr Gly Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met

20

25

30

Ala Glu Gly Cys Gly Ser Lys Glu His Ser Phe Gln His Pro Phe

35

40

45

Leu Gln Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala

50

55

60

Phe Tyr Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Val

65

70

75

80

Asp Pro Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Ala Leu

85

90

95

30 Cys Asp Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr

100

105

110

Ser Ala Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Ile Phe Thr

115

120

125

Gly Leu Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln

130

135

140

Trp Leu Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Val Gly Leu

145

150

155

160

Ala Asp Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val

165

170

175

5 Ile Thr Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile

180

185

190

Gln Met Val Leu Glu Lys Phe Val Tyr Lys His Asn Val His Pro

195

200

205

Leu Arg Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser

210

215

220

Leu Leu Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly

225

230

235

240

Asn Pro Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val

245

250

255

15 Gly Gln Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser

260

265

270

Ile Ala Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser

275

280

285

Ala Thr Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp

290

295

300

Ala Leu Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile

305

310

315

320

Leu Gly Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu

325

330

335

25 His Arg Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu

340

345

350

Glu Ser Glu Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn

355

360

365

Asp Ala Ser

370

&lt;210&gt; 67

&lt;211&gt; 90

&lt;212&gt; PRT

&lt;213&gt; Homo sapiens

71/177

<400> 67  
Met Phe His Gln Ile Trp Ala Ala Leu Leu Tyr Phe Tyr Gly Ile Ile  
1 5 10 15  
5 Leu Asn Ser Ile Tyr Gln Cys Pro Gln His Ser Gln Leu Thr Thr Leu  
20 25 30  
Gly Val Asp Gly Lys Gln Phe Pro Gln Val His Leu Gly Gln Trp Tyr  
35 40 45  
Phe Ile Ala Gly Ala Ala Pro Thr Lys Gln Gln Leu Ala Thr Phe Asp  
50 55 60  
10 Pro Val Asp Asn Ile Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met  
65 70 75 80  
Gln Leu His Leu Arg Ala Thr Ile Arg Met  
85 90  
15  
<210> 68  
<211> 499  
<212> PRT  
<213> Homo sapiens  
20  
<400> 68  
Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu  
1 5 10 15  
Ala Ile Gly Ala Ala Ile Phe Gln Val Leu Gln Gln Pro His Trp Lys  
20 25 30  
Gln Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Gln  
35 40 45  
Phe Pro Cys Leu Gly Gln Gln Gly Leu Asp Lys Ile Leu Gln Val Val  
50 55 60  
30 Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe  
65 70 75 80  
Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile  
85 90 95  
Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg  
100 105 110

72/177

Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr  
115 120 125  
Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Gly Arg Ala Lys Arg Leu  
130 135 140  
6 Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile  
145 150 155 160  
Thr Cys Thr Val Ile Phe Ile Val Trp Gly Val Leu Val His Leu Val  
165 170 175  
10 Ile Pro Pro Phe Val Phe Met Val Thr Gln Gly Trp Asn Tyr Ile Gln  
180 185 190  
Gly Leu Tyr Tyr Ser Phe Ile Thr Ile Ser Thr Ile Gly Phe Gly Asp  
195 200 205  
Phe Val Ala Gly Val Asn Pro Ser Ala Asn Tyr His Ala Leu Tyr Arg  
210 215 220  
15 Tyr Phe Val Gln Leu Trp Ile Tyr Leu Gly Leu Ala Trp Leu Ser Leu  
225 230 235 240  
Phe Val Asn Trp Lys Val Ser Met Phe Val Gln Val His Lys Ala Ile  
245 250 255  
Lys Lys Arg Arg Arg Arg Lys Gln Ser Phe Gln Ser Ser Pro His  
260 265 270  
20 Ser Arg Lys Ala Leu Gln Val Lys Gly Ser Thr Ala Ser Lys Asp Val  
275 280 285  
Asn Ile Phe Ser Phe Leu Ser Lys Lys Gln Gln Thr Tyr Asn Asp Leu  
290 295 300  
25 Ile Lys Gln Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gln  
305 310 315 320  
Thr Gly Pro Gly Pro Gly Leu Gly Pro Gln Gly Gly Gly Leu Pro Ala  
325 330 335  
Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val  
340 345 350  
30 Pro Thr Leu Gln Gln Val Ser Gln Thr Leu Arg Ser Lys Gly His Val  
355 360 365  
Ser Arg Ser Pro Asp Gln Gln Ala Val Ala Arg Ala Pro Gln Asp Ser  
370 375 380  
35 Ser Pro Ala Pro Gln Val Phe Met Asn Gln Leu Asp Arg Ile Ser Gln

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385 390 395 400  
Glu Cys Glu Pro Trp Asp Ala Gln Asp Tyr His Pro Leu Ile Phe Gln  
405 410 415  
Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu  
420 425 430  
Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Ser  
435 440 445  
Pro Gln Gln Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe  
450 455 460  
10 Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser  
465 470 475 480  
Val Pro Tyr Glu Gln Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro  
485 490 495  
Lys Gly Thr  
15  
<210> 69  
<211> 106  
<212> PRT  
20 <213> Homo sapiens  
<400> 69  
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1 5 10 15  
25 Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr Arg Glu Lys Leu Thr Pro  
20 25 30  
Glu Gln Leu His Ser Met Arg Gln Ala Glu Leu Ala Gln Trp Gln Lys  
35 40 45  
Val Leu Pro Arg Arg Arg Thr Arg Asn Ile Val Thr Gly Leu Gly Ile  
50 55 60  
30 Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr Thr Phe Tyr Ser Ile Ser  
65 70 75 80  
Gln Glu Arg Phe Leu Asp Glu Leu Glu Asp Glu Ala Lys Ala Ala Arg  
85 90 95  
35 Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser

100 105  
<210> 70  
<211> 152  
5 <212> PRT  
<213> Homo sapiens  
<400> 70  
Met Asp Tyr Val Cys Cys Ala Tyr Asn Asn Ile Thr Gly Arg Gln Asp  
1 5 10 15  
Glu Thr His Phe Thr Val Ile Ile Thr Ser Val Gly Leu Glu Lys Leu  
20 25 30  
Ala Gln Lys Gly Lys Ser Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile  
35 40 45  
15 Ser Leu Phe Leu Ile Ile Ser Met Cys Leu Leu Phe Leu Trp Lys Lys  
50 55 60  
Tyr Gln Pro Tyr Lys Val Ile Lys Gln Lys Leu Glu Gly Arg Pro Glu  
65 70 75 80  
Thr Glu Tyr Arg Lys Ala Gln Thr Phe Ser Gly His Glu Asp Ala Leu  
85 90 95  
20 Asp Asp Phe Gly Ile Tyr Glu Phe Val Ala Phe Pro Asp Val Ser Gly  
100 105 110  
Val Ser Arg Ile Pro Ser Arg Ser Val Pro Ala Ser Asp Cys Val Ser  
115 120 125  
25 Gly Gln Asp Leu His Ser Thr Val Tyr Glu Val Ile Gln His Ile Pro  
130 135 140  
Ala Gln Gln Gln Asp His Pro Glu  
145 150  
30 <210> 71  
<211> 921  
<212> DNA  
<213> Homo sapiens  
35 <400> 71

75/177

atgctataga ttattatcgc ctatgcatc cgtgtcaag atgactgcg acctctgct 60  
tctactgatt atgacaaag caacaggaatg caagatgtca gaagaattt taantgctt 120  
tcgaggaac ttgtctaac tccatgataa tgtatactga aaactgtaca ttataacatt 180  
aatctatga gctctctgg agtgaactac atgabtgtgt gactgtaaa ttaccgaat 240  
gtctcgcgt tctcttccg gtagagctt cagaaggagt tcaatctac ttataacatg 300  
atgaagacaa atactcgtgt cagacataac tgtttcattg aatttgtaaa cttaataag 360  
aagacaaag agcatatata taatcccaag tctcttcaa caaagataa tctttctgac 420  
atgaagacgg aaatacaagt gagcctcct tatcaattt ccatgtgtga actgtgtgca 480  
gcaaatgtga tcaatcagc atttctcgtt gactgtaaag gtgtgtgaa gatttctct 540  
gtcaacaaag gactgtgaa agaacctctg tcaaggatgt tagaatatt ccttagctt 600  
ttatgtgag cctcgaattt aatcgaagc tttaatgtca tagaaagt cctgaagagt 660  
gtctgtgtatg atttataat cactatgtca ttcttctctg gaacagcagc ctgtcttca 720  
cagtgttaatt taactgtcta ctacacggc tgggtgaatg tcaaatctt tttagattt 780  
ggcttaactc gtctatgcaa catgtatctc tatgaactgc gaacactctg gaacttttc 840  
ttctaatgtga ctgtgtgagc atttgttcaa ctacagatct ggttaagga agccaaaggc 900  
aagctcccg attatgatt c 921

&lt;210&gt; 72

&lt;211&gt; 549

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 72

atgaagccgc aggggggacct gttgtgtcaac cgaagccggc gcttcaagt ggcattgag 60  
ctaagccggc ctggaagagag cagcaggggt cgaagtgaac ggggaagtgg caaggagagc 120  
tcgcctcaac cagtcggtta ctggagcaag caagtgtcctg atacaaggtt gcaagagaaa 180  
gaacggatcc tgggtgagaa ggcgtgtgg gacatgcct tgggtccct caaacagatt 240  
cccatgaaat tcttcatcat gtacatgtga ggtcaatacct tctcatctt cctcatatg 300  
atgtgtgtga tgaatgcctg gcaacccatt caggaaactta tggccatttc agcaatttc 360  
aagatgttaa aaagtcaag ccaagaattt cttaagggtt tggttatcc catgtgaaac 420  
ctgaatgtgt tggatctggc tgtttacaag tgcaggtcaa tgggaatgtt acctaacat 480  
gcatcgaatt gtttagcctt catgtagccc cctgagagaa tgaattcaag tgggtgagga 540  
ctgtcttgc 549

&lt;210&gt; 73

76/177

<211> 981  
<212> DNA  
<213> Homo sapiens

&lt;400&gt; 73

atgagccgc tcccgcggct gctgtgagcc aggggcgtga cggccggct gctctctc 60  
cagtgccttc tgcctgtcgc ggcaccaagc tgggtgagag gcaatgtccc agattgcct 120  
tttaaaagtc caactctcag agaaagata atgcaataa accttccct ggaagatcat 180  
aaatctaac tgaactgaaa ttctagtatg caagttagaa aaatatcaac tttagaaagg 240  
ccttctaag taattctaac atgcagttc aaacatctg gggatttga tgaagttaat 300  
gtgaacttga aaagaatgt tgaacaactt ggaataatt atcttgtcag tgaacagga 360  
agaaacttgt ataccataa cagtttcaac atcatataa gcaacaaat ggaagtatc 420  
tcttgttct ttcgagagga aaagaaaca aggggaactt ttatttcaa agtccctgaa 480  
cttcaatgtga aaacaaagcc atgtatctct taagttaggt atctctactgt ctgaactgt 540  
aaatgtcaaa attgtttcc tttaattgg acctgtgaa gtatgaatgt gactgttaag 600  
gtccctgttg gtttcaaat gaataaatat gttatcaatg gaacataatgc taacgaana 660  
aagctgaaga taacaactt tttagagga gaagggaat cttaactgtg ccgtgtcacta 720  
ttcaaatag gcaagatga agaacactt gactgtgtg tgcgtagata ttgtgtgccc 780  
ctaaacact ttcttgaat agtgcctgag gtgattctt taagtgtcac catcttctt 840  
tgtgaagaat acacacaaa gaaagaagag caatcagatg aggggaagaa atttgagcag 900  
attgaacagc tgaatacaga tgaatgaact ggtatagaaa ataatgtccc caggtataga 960  
aaatgtagt cttcgtgaca g 981

&lt;210&gt; 74

&lt;211&gt; 669

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 74

atgaagctcg tcccctgct cctgtgtgt accttgcct gcttggggac ttgtgtcag 60  
ggcccgagcc aaagaagag aagactggg gaggaaatcc atttccagaa tggagggaaa 120  
gattcctgca ctatgttccc cagcagcttg gggcaagtg ctggaagat ctgtcttgc 180  
gtcgaactgc gcaacaaaga ccaagactac tgggtgtgagt acaagggtgga gscacagatg 240  
tgcgaagctt tgcctgtga cccaactc taactgaac aagccctgga ggaactgag 300  
cgccttcaac atgtgtgca gggggcccg gttattagg cactcgttg caggagagct 360

77/177

6 ggaccacagg cccatagca gcaagtgact tccagctca agggcagccc agagcccac 420  
cagcagctcg aggtctgggac gccatctctg agggcccaagg cccagtgaa actcacgaa 480  
gcacacagc tgggaagga ctgatggaa gactgggaa aagccaaacc caccacccga 540  
cccacagcca aacctaccca gctctggccc aggcacggag ggaatgagga agcaagag 600  
aaggctggg aacattgtg gaacccttc caggccctgt ggcctttct catagcttc 660  
ttccgaggg 669

&lt;210&gt; 75

&lt;211&gt; 144

10 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 75

15 atgagcttc tgcgtctct cctagtggcg gcgtctgca tggtcggag caggcctcg 60  
gccaatctgg gcggcgctgc cagcaagaga ttaagatgc agtacgcc acggcgctg 120  
ctcaagttcc agatttgtg ttcc 144

&lt;210&gt; 76

&lt;211&gt; 1113

20 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 76

25 atggctgga ccaagtacca gctgttctcg gccggggtca tgttgttac cggctccatc 60  
aacacgctct cggcaaatg ggcggacaat ttcatggccg agggctgtgg agggagcaag 120  
gagcacagct tccagatccc ctctctccag gcagtgggca tgttctggg agaatctcc 180  
tgtctggctg cctctacct cctccatgc agagctgcag ggaatcaga ctccagctta 240  
gaccccaagc agcccttcaa cctcttctt ttctggccc cag-gctctg tgacatgaca 300  
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cggggtgag tcatcatatt cactggcctg ttctgggtgg ccttctggg ccggagcty 420  
gtctagccc agtggctggg catctagcc accatgcgg agctgggtgt cgtgggcty 480  
gtcgacctcc ttagcagca cgacagtccg cacaagctca gcgaagtgt cacagggag 540  
ctgttgatca tcatggcca gatcatggt gccatccaga tggctgtaga ggagagttc 600  
gttacaac acaatgca ccaactggg gcagttggca ctgagggct ctttggctt 660  
gtatctct cctgtgtgt ggtgccatg tactacatc ccgcggctc ctccagcga 720

78/177

5 aacctctg ggacactgga ggaatgctg gaagctctt gccaggtgg ccagcagcag 780  
ctcatctcg tggcaatgct gggcaacatc agcagcttg ccttcttcaa ctccagggc 840  
atcagctca ccaaggaact gacgcaccc accgcctgg tgttgacag cttagcacc 900  
gttctctct gggcactgag cctggcactg ggtggggagg ccttcctatg actgcagatc 960  
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ctggggcgcc tgcacagggg ccggccctg gcagaggaga gcgacagga gagactgtg 1080  
ggtggcacc gactctcat caatgatgc agc 1113

&lt;210&gt; 77

10 &lt;211&gt; 270

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 77

15 atgttccac aatttgggc agctctgct tactctatg gtattactc taactccatc 60  
taccagccc ctggacacag tcaactgaca actctggcg tggatggaa ggaattccca 120  
gagttcaact tgggcaatg gtaatttato gcaggggag ctcccacaa ggagaggtg 180  
gcaactttg acctatgga caacattgct ttaatatgg ctgtgtgctc tgcacagatg 240  
cagttccac ttctgtctac catccgcatg 270

&lt;210&gt; 78

&lt;211&gt; 1497

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 78

25 atggtggacc ggggcctct gctcacctcg gccatcatct tctacctgga catcggggag 60  
gcgattctcg aagtgtgga ggaacacac tggagggagg ccaagaaaa ctactacaa 120  
cagaagctgc atctgtcaa ggaattcccg tgcctgggic agggggcct ggacagatc 180  
ctagaggtgg tatctatgc tgaaggacag ggtgtggcca tcaagggaa ccagacctc 240  
aacactgga actggccaa tgaatgat tttagcaga cgtctctac caccattgga 300  
tatggcaatg tggctccaa gacccccc ggtgcctct tctgtgtt ctatggtctc 360  
ttcggggctg cgtctgctt gacgtggtc agtgcctgg gcaagtctt cgggggagct 420  
gcacagagac tagggagtt ccttaccag agaggtgtga gtctgggaa ggcgcagatc 480  
acgtgcacag taactctat cgtgtgggg gtcctagtc acctgtgat cccaccttc 540



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gtattcatg tgaactagg gtgaaactac atcgagggc tactactac ctctacacc 600  
atctccacca tccgtctcgg tgactttgtg gacgtgtga accccaagcg caactcaaac 660  
gacctgacc gactactcgt ggaagctatg actacttgg ggttggctg gcttccact 720  
ttgtccact ggaagttgag catgtttgtg gaagtcaca aagcattaa gaagcgggg 780  
cggtgaaaga aagagctcct tgaagctac ccaactccc ggaagggcct gacgttgaag 840  
ggagacacag cctccaaagg cgtcaacatc tcaagttta ttccaaaga ggaagagacc 900  
tacaacgacc tcaacaaga gaccgggag aagcocatga agacaagcg ggttggggag 960  
aagggcccg gacaaaggct ggggctcaa ggggttggc tcccaagact gacctctcc 1020  
ctgtgtccc tggatgcta atccaaagac cgggttgcna ccttggaga ggtgtcacg 1080  
acactgaga gcaagggcca cgtatcaag tcccagatg aggaagctgt ggcaggggc 1140  
cctgaagaca gctccctgc ccccgaggtg ttaatgaac agctggaccg catcaagag 1200  
gaatcgagag catggagcgc ccaagactac caacactaa tcttcagga cgcagacac 1260  
accttcgtga acacggagagc tggctctca gaagagaga cctccagtc ctgcctag 1320  
gcaacttgg cagggagaga gaggcccaag cagggggctg aagcaagagc gacctgaac 1380  
atgggcagat tccctctcc ctccaggtcc acctcaaaa gaactgaagc tgaactctc 1440  
gtgcttacc aacagctgat gaatgaatc acaagagcta aacgcccna ggggaca 1497

<210> 79  
<211> 318  
<212> DNA  
<213> Homo sapiens

<400> 79  
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cagcgtatcg acccgactcg ggaagagctg aaacccagag aactgaatic catcgagcag 120  
ggcggcttg cccagtgaga gaagtccta ccaagggcgc gaaccggaa catcgtgaac 180  
ggcgaagga tccggccct ggtgttggct atttatggt aacacttca ctcgaattcc 240  
cagagcgtt tccatagta gctagaagc gaggaagag ctgcaggagc ccgagctctg 300  
gcagagcgt ccgggtcc 318

<210> 80  
<211> 456  
<212> DNA  
<213> Homo sapiens

35

80/177

<400> 80  
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aacgtatca tcaattcgt aggaactggag aagcttgcac agaaaggaaa atcattgtca 120  
ccttgaaga gtaaacatg aatcacctta tttttgatta tatccatgtg tcttccttc 180  
ctatgaaaa aatatcaacc ctacaaggt ataaacaga aactagaagc cagggcagaa 240  
acagataca ggaagctca aacttttca ggcacatgag atgcttga tgacttcgga 300  
atatgaat ttgttgcct tccagatgt tctgtgttt ccagatccc aagcaggtct 360  
gttccagct ctgatttgt atcgggcaa gatttgaca gtacagctga tgaagtatt 420  
cagcacctac ctgcacagca gaagacatc ccaagag 456

<210> 81  
<211> 1436  
<212> DNA  
<213> Homo sapiens  
<220>  
<221> CDS  
<222> (66)...(989)

<400> 81  
gaactcgg ggcgtcact cggagcggcg gttcccgctc cgaagctct tctcgttgg 60  
ttgaa atg tct atg att ita tct gcc tca gtc att cgt gtc aga gat 107  
Met Ser Met Ile Leu Ser Ala Ser Val Ile Arg Val Arg Asp  
1 5 10

gga ctg cca ctt tct gct tct act gat tat gaa caa agc aca gga atg 155  
Gly Leu Pro Leu Ser Ala Ser Thr Asp Tyr Glu Gln Ser Thr Gly Met  
15 20 25 30  
cag gag tgc aga aag tat ttt aaa atg ctt tcg agg aaa ctt gct caa 203  
Gln Glu Cys Arg Lys Tyr Phe Lys Met Leu Ser Arg Lys Leu Ala Gln  
35 40 45

ctt cct gat aga tgc aca ctg aaa act gga cat tat aac att aat ttt 251  
Leu Pro Asp Arg Cys Thr Leu Lys Thr Gly His Tyr Asn Ile Asn Phe  
50 55 60  
att agc tct ctg gga gtc agc tac atg atg ttg tgc act gaa aat tac 299  
Ile Ser Ser Leu Gly Val Ser Tyr Met Met Leu Cys Thr Glu Asn Tyr  
65 70 75

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255 260 265 270 285  
 tat gaa ctg cgc aac ctc tgg cag ctt ttc ttt cct gtc act gtc gga  
 Tyr Glu Leu Arg Asn Leu Trp Gln Phe Phe His Val Thr Val Gly  
 275 280 285  
 5 gca ttt gtt aca cta cag atc tgg cta agg oaa gcc cag ggc aag gct  
 Ala Phe Val Thr Leu Gln Ile Trp Leu Arg Gln Ala Gln Gly Lys Ala  
 290 295 300  
 ccc gat tat gat gtc tgaaccatc cttaagatct attgcttgg ettc  
 Pro Asp Tyr Asp Val  
 305  
 10 agggggataa ggagggaaca tatcataact gaactgtgat gaagaagctg ttccccacag  
 aggaagct ctgctttctt tctctcaac ttctctttt taaaatcagc atgctgtgac  
 tctgagcatg gaagagctct ctcaagaaga tcttggaat gaactatca ttcaagaggag  
 gagggatt ctctcttcaa ggcataaaca ggggaagac agtcatatgc catgggaagt  
 ctggccagc agtctgaat ccttctgaa gacttcagaa aatagatgtg gtattgtctt  
 gaggaacagg caggaggaaac tctcaacct gacttggct tctgaggca ttagtataga  
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 cgaggctata ggacgagct gttgcc atg acg gcc cag ggc ctc gtc gtc  
 Met Thr Ala Gln Gly Leu Val  
 1 5  
 gct aac cga ggc cgc ttc aag tgg gcc att gag cta agc ggg cct  
 Ala Asn Arg Gly Arg Arg Phe Lys Trp Ala Ile Glu Leu Ser Gly Pro  
 10 15 20  
 gga gga ggc agc agg ggt cga agt gac cgg ggc agt ggc cag gga gac  
 35 206

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347 395 443 491 539 587 635 683 731 779 827 875  
 cca aat gtt ctc gcc ttc ttc ttc ctg gat gag ctt cag aag gag ttc  
 Pro Asn Val Leu Ala Phe Ser Phe Leu Asp Glu Leu Gln Lys Glu Phe  
 80 85 90  
 att act act tat aac atg atg aag aca aat act gtc aga cca tac  
 Ile Thr Thr Tyr Asn Met Met Lys Thr Asn Thr Ala Val Arg Pro Tyr  
 95 100 105 110  
 tgc ttc att gaa ttt gat aac ttc att cag agg acc aag cag cga tat  
 Cys Phe Ile Glu Phe Asp Asn Phe Ile Gln Arg Thr Lys Gln Arg Tyr  
 115 120 125  
 10 aat aat ccc agg tct ctt tca aca aag ata aat ctt tct gac atg cag  
 Asn Asn Pro Arg Ser Leu Ser Thr Lys Ile Asn Leu Ser Asp Met Gln  
 130 135 140  
 acg gaa atc aag ctg agg cct cct tat cca att tcc atg tgc gaa ctg  
 Thr Glu Ile Lys Leu Arg Pro Pro Tyr Gln Ile Ser Met Cys Glu Leu  
 145 150 155  
 ggg tca gcc aat gga gtc aca tca gca ttt tct gtt gac tgt aaa ggt  
 Gly Ser Ala Asn Gly Val Thr Ser Ala Phe Ser Val Asp Cys Lys Gly  
 160 165 170  
 get ggt aag att tct tct gct cac cag cga ctg gaa cca gca act ctg  
 Ala Gly Lys Ile Ser Ser Ala His Gln Arg Leu Glu Pro Ala Thr Leu  
 175 180 185 190  
 tca ggg att gta gga ttt atc ctt agt ctt tta tgt gga get ctg aat  
 Ser Gly Ile Val Gly Phe Ile Leu Ser Leu Leu Cys Gly Ala Leu Asn  
 195 200 205  
 25 tta att cga ggc ttt cat gct ata gaa agt ctc ctg cag agt gat ggt  
 Leu Ile Arg Gly Phe His Ala Ile Glu Ser Leu Leu Gln Ser Asp Gly  
 210 215 220  
 gat gat ttt aat tac atc att gca ttt ttc ctt gga aca gca gcc tgc  
 Asp Asp Phe Asn Tyr Ile Ile Ala Phe Phe Leu Gly Thr Ala Ala Cys  
 225 230 235  
 30 ctt tac cag tgt tat tta ctt gtc tac tac acc ggc tgg cgg aat gtc  
 Leu Tyr Gln Cys Tyr Leu Leu Val Tyr Tyr Thr Gly Trp Arg Asn Val  
 240 245 250  
 aaa tct ttt ttg act ttt ggc tta atc tgt cta tgc aac atg tat ctc  
 Lys Ser Phe Leu Thr Phe Gly Leu Ile Cys Leu Cys Asn Met Tyr Leu  
 255 260 265 270 275 280 285 290 295 300 305 310 315 320 325 330 335 340 345 350 355 360 365 370 375 380 385 390 395 400 405 410 415 420 425 430 435 440 445 450 455 460 465 470 475 480 485 490 495 500 505 510 515 520 525 530 535 540 545 550 555 560 565 570 575 580 585 590 595 600 605 610 615 620 625 630 635 640 645 650 655 660 665 670 675 680 685 690 695 700 705 710 715 720 725 730 735 740 745 750 755 760 765 770 775 780 785 790 795 800 805 810 815 820 825 830 835 840 845 850 855 860 865 870 875 880 885 890 895 900 905 910 915 920 925 930 935 940 945 950 955 960 965 970 975 980 985 990 995

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Gly Gly Ser Arg Gly Arg Ser Asp Arg Gly Ser Gly Gln Gly Asp  
 25 30 35 40  
 tcc ctc tac cca gtc ggt tac ttg gac aag caa gtc cct gat acc agc  
 Ser Leu Tyr Pro Val Gly Tyr Leu Asp Lys Gln Val Pro Asp Thr Ser  
 45 50 55  
 gtg caa gag aca gac cgg atc ctg gtc gag aag cgc tgc tgg gac atc  
 Val Gln Gln Thr Asp Arg Ile Leu Val Gln Lys Arg Cys Trp Asp Ile  
 60 65 70  
 gcc ttg ggt ccc ctc aaa cag att ccc atg aat ctc ttc atc atg tac  
 10 Ala Leu Gly Pro Leu Lys Gln Ile Pro Met Asn Leu Phe Ile Met Tyr  
 75 80 85  
 atg gca ggc aat act atc tcc atc ttc cct act atg atg gtc tgt atg  
 Met Ala Gly Asn Thr Ile Ser Ile Phe Pro Thr Met Met Val Cys Met  
 90 95 100  
 atg gcc tgg cga ccc att cag gca cit atg gcc att tca gcc act ttc  
 15 Met Ala Trp Arg Pro Ile Gln Ala Leu Met Ala Ile Ser Ala Thr Phe  
 105 110 115 120  
 aag atg tta gaa agt tca agc cag aag ttt ctt cag ggt ttg gtc tac  
 Lys Met Leu Gln Ser Ser Ser Gln Lys Phe Leu Gln Gly Leu Val Tyr  
 125 130 135  
 ctc att ggg aac ctg atg ggt ttg gca ttg gct gtt tac aag tgc cag  
 Leu Ile Gly Asn Leu Met Gly Leu Ala Leu Ala Val Tyr Lys Cys Gln  
 140 145 150  
 tcc atg gga ctg tta cct aca cat gca tcc gat tgg tta gcc ttc att  
 25 Ser Met Gly Leu Leu Pro Thr His Ala Ser Asp Trp Leu Ala Phe Ile  
 155 160 165  
 gag ccc cct gag aga atg gag ttc agt ggt gga gga ctg ctt ttg tgaac  
 Gln Pro Pro Gln Arg Met Gln Phe Ser Gly Gly Leu Leu Leu  
 170 175 180  
 atgagaagc agcgctcgtt cccatgcat ttgggtctta ttacatcct tctttaagcc  
 30 cagtgctcc tcaagatact cttaactaa tcaatttgt taagaagac caaagctcc  
 ttctccat ggtgggtga caggtccctag aaggaacatg tgcatttac gaaacacaa  
 aagaactat accataacc aaggtcgaa ataatgtaga aaacttaatt ttgtttcca  
 gtaagagca aanaaacaac aaaaaaacat aaactgtaa acaaggaat aactgtcgt  
 35 aatacaaga atgtgtgagc atctccttc aataaatlaa atgtgtgaga acaatgc  
 700 760 820 880 940 997

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 60 ggaactctg acaaccgag cggagagctg agggagagat ctcacagagg accaagcgg  
 120 accctctgac gcc atg cgc gcc ctc ccc ggc ctg gtc ggc agt ggc  
 169 Met Arg Ala Leu Pro Gly Leu Leu Gln Ala Arg Ala  
 15 1 5 10  
 cgt acg ccc cgg ctg ctc ctc ctc cag tgc ctt ctc gtc gcc ggc cgc  
 Arg Thr Pro Arg Leu Leu Leu Leu Gln Cys Leu Leu Ala Ala Arg  
 15 20 25  
 cca agc tgg gcg gac ggc agt gcc cca gat tgg cct ttt aca agt cca  
 20 Pro Ser Ser Ala Asp Gly Ser Ala Pro Asp Ser Pro Phe Thr Ser Pro  
 30 35 40  
 cct ctc aga gaa gaa ata atg gca aat aac ttt tcc ttg gag agt cat  
 Pro Leu Arg Gln Gln Ile Met Ala Asn Asn Phe Ser Leu Gln Ser His  
 45 50 55 60  
 aac ata tca ctg act gaa cat tct agt atg cca gta gaa aat atc  
 25 Asn Ile Ser Leu Thr Gln His Ser Ser Met Pro Val Gln Lys Asn Ile  
 65 70 75  
 act tta gaa agg cct tct aat gta aat ctc aca tgc cag ttc aca aca  
 Thr Leu Gln Arg Pro Ser Asn Val Asn Leu Thr Cys Gln Phe Thr Thr  
 80 85 90  
 tct ggg gat ttg aat gca gta aat gtc act tgg aaa aaa ggt gaa  
 Ser Gly Asp Leu Asn Ala Val Asn Val Thr Trp Lys Lys Asp Gly Gln  
 95 100 105  
 caa ctt gag aat aat tat ctt gtc agt gca aca gga agc acc ttg tat  
 35 Gln Leu Gln Asn Asn Tyr Leu Val Ser Ala Thr Gly Ser Thr Leu Tyr  
 505

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110 115 120  
acc caa tac egg ttc acc att aat agc aaa caa atg gga agt tat 553  
Thr Gln Tyr Arg Phe Thr Ile Ile Asn Ser Lys Gln Met Gly Ser Tyr 140  
125 130 135  
tct tgt ttc ttt cga gag gaa aag gaa caa egg gga aca ttt aat ttc 601  
Ser Cys Phe Phe Arg Glu Glu Lys Glu Arg Gly Thr Phe Asn Phe 155  
145 150 155  
aaa gtc cct gaa ctt cat ggg aaa aac aag cca ttg atc tct tac gta 649  
Lys Val Pro Glu Leu His Gly Lys Asn Lys Pro Leu Ile Ser Tyr Val 170  
160 165 170  
ggg gat tct act gtc ttg aca tgt aaa tgt caa aat tgt ttt cct tta 697  
Gly Asp Ser Thr Val Leu Thr Cys Lys Cys Gln Asn Cys Phe Pro Leu 185  
175 180 185  
aat tgg acc tgg tac agt agt aat ggg agt gta aag gtt cct gtt ggt 745  
Asn Trp Thr Trp Tyr Ser Ser Asn Gly Ser Val Lys Val Pro Val Gly 200  
190 195 200  
gtt caa atg aat aaa tat gtg atc aat gga aca tat gct aac gaa ace 793  
Val Gln Met Asn Lys Tyr Val Ile Asn Gly Thr Tyr Ala Asn Glu Thr 215  
205 210 215  
aag ctg aag ata aca caa ctt ttg gag gaa gat ggg gaa tct tac tgg 841  
Lys Leu Lys Ile Thr Gln Leu Leu Glu Glu Asp Gly Glu Ser Tyr Trp 230  
225 230 235  
tgc cgt gca cta ttc caa tta ggc gag agt gaa gaa cac att gag ctt 889  
Cys Arg Ala Leu Phe Gln Leu Gly Glu Ser Glu Glu His Ile Glu Leu 250  
240 245 250  
gtg gtg ctg agc tat ttg gtg ccc ctc aaa cca ttt ctt gta ata gtg 937  
Val Val Leu Ser Tyr Leu Val Pro Leu Lys Pro Phe Leu Val Ile Val 265  
255 260 265  
ggt gag gtg att ctt tta gtg gcc acc att ctg ctt ttg gaa aag tac 985  
Ala Glu Val Ile Leu Leu Val Ala Thr Ile Leu Leu Cys Glu Lys Tyr 280  
270 275 280  
aca caa aag aaa aag aag cac tca gat gag ggg aaa gaa ttt gag cag 1033  
Thr Gln Lys Lys Lys His Ser Asp Glu Gly Lys Glu Phe Glu Gln 295  
285 290 295  
att gaa cag ctg aaa tca gat gat agc aat ggt ata gaa aat aat gtc 1081

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110 115 120  
ile Glu Gln Leu Lys Ser Asp Asp Ser Asn Gly Ile Glu Asn Asn Val 315  
305 310 315  
ccc egg cat aga aaa aat gag tct ctg ggc cag tgaatacaaa acatca 1130  
Pro Arg His Arg Lys Asn Glu Ser Leu Gly Gln 325  
320 325  
tgtgagaat cattggaaga tacaagagt tegtatttca gtttattta tecttctgt 1190  
taagagctc tgagttttta gttttaaaag gatgaaagc ttatgaaaca tgcacagcag 1250  
gagcttacc aacgatataat gtcagatcta aaggtatatt ttoatttgt aattatgta 1310  
cataaagca atgtaataca gaataaatat gtagaccag aataaatta attatattct 1370  
ggcttcaaa ggacacacag aacagatatac agcagaatca cttaatactt catagaacaa 1430  
aaatcacata aaactgtttt ataaccaag aattcatgaa aagaaagcc ttggcattt 1490  
gcttagaaa gttatttttt taanaaaat catacttact attagtatct atggagatat 1550  
agtaaacat ttattatgtaa aggtcatctt tctgtgatag tgaanaata tgcctttact 1610  
aagttgaat gaatacttcc tgcctttgct catgatagtt atttacaat ctccacaaga 1670  
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ctaaagctct gcactacaaa agc 1753

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Met Lys Phe Val Pro Cys Leu Leu Val Thr Leu Ser Cys Leu 15  
1 5 10 15  
ggg act ttg ggt cag gcc ccg agg caa aag caa gga agc act ggg gag. 154  
Gly Thr Leu Gly Gln Ala Pro Arg Gln Lys Gln Gly Ser Thr Thr Gly Glu 20  
25 30  
gaa ttc cat ttc cag act gga ggg aga gat tcc tgc act atg cgt ccc 202  
Glu Phe His Phe Gln Thr Gly Arg Asp Ser Cys Thr Met Arg Pro 35

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35 40 45  
agc agc ttg ggg caa ggt gct gga gaa gtc tgg ctt cgc gtc gac tgc 250  
Ser Ser Leu Gly Gln Gly Ala Gly Gln Val Trp Leu Arg Val Asp Cys  
50 55 60  
cgc aac aca gac caa acc tac tgg tgt gag tac agg ggg gac cgc agc 298  
Arg Asn Thr Asp Gln Thr Tyr Trp Cys Gln Tyr Arg Gly Gln Pro Ser  
65 70 75  
atg tgc cag gct ttc gct gct gac ccc aac tct tac tgg aat caa gcc 346  
Met Cys Gln Ala Phe Ala Ala Asp Pro Lys Ser Tyr Trp Asn Gln Ala  
80 85 90 95  
ctg cag gag ctg agg cgc ctt cac cat gcg tgc cag ggg gcc ccg gtg 394  
Leu Gln Gln Leu Arg Arg Leu His His Ala Cys Gln Gly Ala Pro Val  
100 105 110  
ctt agg cca tcc gtg tgc agg gag gct gga ccc cag gcc cat atg aag 442  
Leu Arg Pro Ser Val Cys Arg Gln Ala Gly Pro Gln Ala His Met Gln  
115 120 125  
cag gtg act tcc agc ctg aag ggc agc cca gag ccc aac cag cag cct 490  
Gln Val Thr Ser Ser Leu Lys Gly Ser Pro Gln Pro Asn Gln Pro  
130 135 140  
gag gct ggg acg cca tct ctg agg gcc aag gcc aca gtg aaa ctg aca 538  
Glu Ala Gly Thr Pro Ser Leu Arg Pro Lys Ala Thr Val Lys Leu Thr  
145 150 155  
gaa gca aca cag ctg gga aag gac tcg atg gaa gag ctg gga aaa gcc 586  
Glu Ala Thr Gln Leu Gln Lys Asp Ser Met Gln Gln Leu Gly Lys Ala  
160 165 170 175  
aaa ccc acc acc cga ccc aca gcc aaa cct acc cag cct gga ccc agg 634  
Lys Pro Thr Thr Arg Pro Thr Ala Lys Pro Thr Gln Pro Gly Pro Arg  
180 185 190  
ccc gga ggg aat gag gaa gca aag aag aag gcc tgg gaa cat tgt tgg 682  
Pro Gly Gly Asn Gln Gln Ala Lys Lys Lys Ala Trp Gln His Cys Trp  
195 200 205  
aaa ccc ttc cag gcc ctg tgc gcc ttt ctg atc agc ttc ttc cga ggg 730  
Lys Pro Phe Gln Ala Leu Cys Ala Phe Leu Ile Ser Phe Arg Arg Gly  
210 215 220  
tgcaggtga aagacccta cagatctgac ctctccctga cagacaacca tctcttttta 790

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tattatgag ctccaatcc aactgtcca caatggaaga agagagtttc taatgaatg 850  
caacggccca aattctgat ctgcagcttc tcgaagttt ggaagaana ccttccttc 910  
tgaagtttgc agagttcagc aatatgatag ggaacaggtg ctgatgggc caagatgac 970  
aagctacac aactactat tatctgaga agtttgtct tgtgactg agccttcct 1030  
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Met Arg Leu Leu  
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ctg ctt ctg cta gtc ggc ggc tct gcg atg gtc cgg agc gag gcc tgg 102  
Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Gln Ala Ser  
5 10 15 20  
gcc aat ctg ggc ggc gtc ccc agc aag aga tta aag atg cag tac gcc 150  
Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala  
25 30 35  
aag ggg ccg ctg ctg aag ttc cag att tgt gtt tcc tgaag 190  
Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser  
40 45  
gtataggcg ggtgtttgag gactacatgc ggttatatg coagcgttac ccagacatcc 250  
gacttgaag agagaattac ctccctcaac caataatag acacatagca tcttcctgt 310  
cagttcca aactagtatc atagcttaa taattgttg caagatcct ttgtcttct 370  
ttggcatgca agtctcagc atctgcagt ggggcacaga aataaaggt tatgatgta 430  
tgatgttt ctcttgagc aacatgalt agaacagtg tatgcaaca ggtgatgtt 490  
agataacttt aatgatgta cctgtgtgt ctaagctgga atctgttacc ctccatcca 550  
tgaacaact tgtcaact ctgacaatg aatgaagct caatgtgat atgatccaa 610

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248 gaa gta ggc atg ttc ctg gga gaa ttc tcc tgc ctg gct gcc ttc tac  
 Ala Val Gly Met Phe Leu Gly Glu Phe Ser Cys Leu Ala Ala Phe Tyr  
 55 60 65  
 296 ctc ctc cga tgc aga gct gca ggg caa tca gac tcc agc gta gac ccc  
 Leu Leu Arg Cys Arg Ala Ala Gly Gln Ser Asp Ser Ser Val Asp Pro  
 70 75 80  
 344 cag cag ccc ttc aac cct ctt ctt ttc ctg ccc cca gcg ctc tgc gac  
 Gln Gln Pro Phe Asn Pro Leu Leu Phe Leu Pro Ala Leu Cys Asp  
 85 90 95  
 392 atg aca ggg acc age ctc atg tat gta gct ctg aac atg acc agt gcc  
 Met Thr Gly Thr Ser Leu Met Tyr Val Ala Leu Asn Met Thr Ser Ala  
 100 105 110  
 440 tcc agc ttc cag atg ctg cgg ggt gca gta atc ata ttc act ggc ctg  
 Ser Ser Phe Gln Met Leu Arg Gly Ala Val Ile Phe Thr Gly Leu  
 115 120 125 130  
 488 ttc tgc gta gcc ttc ctg ggc cgg agg ctg gta ggc cag tgg ctg  
 Phe Ser Val Ala Phe Leu Gly Arg Arg Leu Val Leu Ser Gln Trp Leu  
 135 140 145  
 536 ggc atc cta gcc acc atc gta ggg ctg gta gta ggc ctg gct gcc  
 Gly Ile Leu Ala Thr Ile Ala Gly Leu Val Val Gly Leu Ala Asp  
 150 155 160  
 584 ctc ctg agc aag cag cag cag cag cag cag cag gaa gta atc aca  
 Leu Leu Ser Lys His Asp Ser Gln His Lys Leu Ser Glu Val Ile Thr  
 165 170 175  
 632 ggg gac ctg tta atc atc atg gcc cag atc atc gtt gcc atc cag atg  
 Gly Asp Leu Leu Ile Ile Met Ala Gln Ile Ile Val Ala Ile Gln Met  
 180 185 190  
 680 gta cta gag gag aag ttc gta tac aca cag aat gta cca cca ctg egg  
 Val Leu Glu Glu Lys Phe Val Tyr Lys His Asn Val His Pro Leu Arg  
 195 200 205 210  
 728 gca gtt ggc act gag ggc ctc ttt ggc ttt gta atc ctc tcc ctg ctg  
 Ala Val Gly Thr Glu Gly Leu Phe Gly Phe Val Ile Leu Ser Leu Leu  
 215 220 225  
 776 cta gta ccc atg tac tac atc ccc gcc ggc tcc ttc agc gga aac cct  
 Leu Val Pro Met Tyr Tyr Ile Pro Ala Gly Ser Phe Ser Gly Asn Pro  
 230 235 240

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670 tccacaccca tgcatacatg caccacccat cagcactgaa aactcttttg cattaaaggga  
 730 tcatgcaag agcagcgctga ctgacattat gaagcgctgt actgaagaca gcaagcgtt  
 790 agtaacagcc agatgcttgc ttggcaggct cgtgtacct ctggaanaa ctaaatgcaa  
 850 gatagttt cagtgctgga atatttggga attctgaca ttaatgaggt gcaataatac  
 910 tgaatagtt tcccacaccc ccaacaaac acccagttaa tgaatgctg tttttttt  
 970 ttttaaggtaa acattactac ttgtaacttt tttcttagt catattttaa aaagtgaana  
 1030 attgagttac aatttgattt ttttccaaa gatgtctgtt aaatctgtg tgcatttata  
 1090 tgaatatttg tttttatag tttaaaattg atccttggg aatccagttg aagttccaaa  
 1150 atactttata agagttttatc agacatctct aatttgcca tgcacagttt ataacgttta  
 1210 caaaatatag cagatgcagc attatgggg aaatctata ttaaggtac tctataaatt  
 1270 tttgtgatg tgtgtgatg cgtgtgatta ccagagaact actaaanaa ccaactgctt  
 1330 ttttaactct attgtgaggt taaagtga tgcctgacc aatataaga attgattaat  
 1380 taactgggcc tttatactta actaaataaa aaactaagca gatagagtt  
  
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 Trp Thr Lys Tyr Gln Leu Phe Leu Ala Gly Leu Met Leu Val Thr Gly  
 5 10 15  
 30 tcc atc aac acg ctc tgc gca aca tgg ggc gac aat ttc atg gcc gag  
 Ser Ile Asn Thr Leu Ser Ala Lys Trp Ala Asp Asn Phe Met Ala Glu  
 20 25 30  
 200 ggc tgt gga ggg agc aag gag cac agc ttc cag cat ccc ttc ctc cag  
 Gly Cys Gly Gly Ser Lys Glu His Ser Phe Gln His Pro Phe Leu Gln  
 35 40 45 50

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230 235 240  
cgt ggg aca ctg gag gat gaa ttg gac ggc ttc tgc cag gtg ggc aag 824  
Arg Gly Thr Leu Glu Asp Ala Leu Asp Ala Phe Cys Gln Val Gly Gln  
245 250 255  
cag ccg ctc att gcc ctg gca ctg ggc aac atc agc agc att gcc 872  
Gln Pro Leu Ile Ala Val Ala Leu Leu Gly Asn Ile Ser Ser Ile Ala  
260 265 270  
ttc ttc aac ttc gca ggc atc agc gtc aac aag gaa ctg agc ggc aac 920  
Phe Phe Asn Phe Ala Gly Ile Ser Val Thr Lys Glu Leu Ser Ala Thr  
275 280 285 290  
acc cgc atg gtc tgc gac agc ttg cgc acc gtc atc tgg gca ctg 968  
Thr Arg Met Val Leu Asp Ser Leu Arg Thr Val Val Ile Trp Ala Leu  
295 300 305  
agc ctg gca ctg ggc tgg gag ggc ttc cat gca ctg cag atc ctt ggc 1016  
Ser Leu Ala Leu Gly Trp Glu Ala Phe His Ala Leu Gln Ile Leu Gly  
310 315 320  
ttc ctc ata ctc ctt ata ggc act gcc ctc tac aat ggg cta cac cgt 1064  
Phe Leu Ile Leu Leu Ile Gly Thr Ala Leu Tyr Asn Gly Leu His Arg  
325 330 335  
ccg ctg ctg ggc cgc ctg tcc aag ggc cgg ccc ctg gca gag gag agc 1112  
Pro Leu Leu Gly Arg Leu Ser Arg Gly Arg Pro Leu Ala Glu Glu Ser  
340 345 350  
gag cag gag aga ctg ggt ggc acc cgc act ccc atc aat gat gcc 1160  
Gln Gln Glu Arg Leu Leu Gly Gly Thr Arg Thr Pro Ile Asn Asp Ala  
355 360 365 370  
agc tgaagttccc tgaaggtctc taactgcaac cgggtgtctcc ttctccc 1210  
Ser  
tgaagctgag gcaacacagc ctgtgtggcc ccgaatggcc tatcccaag gctcaccct 1270  
gtcccccacc tgcagaaacc ccagggcagc tgcctgcaca gaagataaca acaaccagct 1330  
ccctctttc taactaacac ctgaagggtg gttgtaccac gcccccacaa gcttgagtcg 1390  
agtgacacac cccagctctc tgaaccctcc ctacagacct agagctaat catgaagttg 1450  
aatgtatgga atttaccac gtaagtatc tgaataataa actagattat cat 1503

35 &lt;210&gt; 87

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<211> 733  
<212> DNA  
<213> Homo sapiens  
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<221> CDS  
<222> (40)...(312)  
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Met Phe His Gln Ile  
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tgg gca gct ctg ctc tac ttc tat ggt att atc ctt aac tcc atc tac 102  
Trp Ala Ala Leu Leu Tyr Phe Tyr Gly Ile Ile Leu Asn Ser Ile Tyr  
10 15 20  
cag tgc cct gag aac agt caa ctg aca act ctg ggc gtc gat ggg aag 150  
Gln Cys Pro Glu His Ser Gln Leu Thr Leu Gly Val Asp Gly Lys  
25 30 35  
gag ttc cca gag gtc cac ttg ggc cag tgg tac ttc atc gca ggg gca 198  
Gln Phe Pro Glu Val His Leu Leu Gly Gln Trp Tyr Phe Ile Ala Gly Ala  
40 45 50  
gct ccc acc aag gag gag ttg gca act ttt gac cct gtc gac aac att 246  
Ala Pro Thr Lys Lys Glu Glu Leu Ala Thr Phe Asp Pro Val Asp Asn Ile  
55 60 65  
gtc ttc aat atg gct gct ggc tct gcc ccg atg cag ctc cac ctt cgt 294  
Val Phe Asn Met Ala Ala Gly Ser Ala Pro Met Gln Leu His Leu Arg  
70 75 80 85  
gct aac atc cgc atg tgaatgaaa gatgggtctc gttgtgcccg g 340  
Ala Thr Ile Arg Met  
90  
aatgtatct accacactgac tgaagggagc acagatctca gaactgaag ccgacctgac 400  
atgaagctg agctctttc cagtcatgc ccaggttgaa tcatgttga tgaagacaggc 460  
ccaggttacc agcgtttct cctctacaat cgttaccac atccctccga aaagtgtgtg 520  
gggaattca agtccctgac ttctgtctg gactacaag cctcttatt gactcctagg 580  
aatcaagag ccctgtgagc gtcaatlaac tgacctgaa cttaactcaa gtcccccagat 640  
gggtcaaatg gtagctgagc tgttggaggg agaaagctga gacttcagc tccagctccc 700

actcaagata ataaagataa ttttcaate ctc	733	Asn Asn Trp Asn Trp Pro Asn Ala Met Ile Phe Ala Ala Thr Val Ile	85	90	95
<210> 88		acc acc att gga tat ggc aat gtc gct ccc aag acc ccc gcc ggt cgc			693
<211> 3768		Thr Thr Ile Gly Tyr Gly Asn Val Ala Pro Lys Thr Pro Ala Gly Arg			
<212> DNA		ctc ttc tgt gtt ttc tat ggt ctc ttc ggg gtc cgc ctc tgc ctg acg	100	105	110
<213> Homo sapiens		Leu Phe Cys Val Phe Tyr Gly Leu Phe Gly Val Pro Leu Cys Leu Thr			741
<220>		tgg atc agt gcc ctg ggc aag ttc ttc ggg gga cgt gcc aag aga cta	115	120	125
<221> CDS		Trp Ile Ser Ala Leu Gly Lys Phe Phe Gly Arg Ala Lys Arg Leu			789
<222> (358)...(1857)		ggg cag ttc ctt acc aag aga ggt gtc agt ctg cgc aag ggc cag atc	130	135	140
<400> 88		Gly Gln Phe Leu Thr Lys Arg Gly Val Ser Leu Arg Lys Ala Gln Ile			837
gctagtggcg cgcgagggag cgaacgtgg agaacggcc cactgtcttg cccagagtaa	50	145	150	155	160
agtcctgtgt tcttcagcgt ccttaacgat ccgcgttcca gggcgccctt tcagcccgcc	120				
tgggtgtcgc ccaccccggg ccgcgtgagt gggggcccaac gcaagtcacc gcactccgtg	180				
ggccaaacttg gccaaagcaac tctgtccggg gacggtggt tggggggggt gactaccggg	240				
cactgcgat gcggagatcc aaattcaaac agctgttttc agagcttga gggcgggcgg	300				
actgttagca gctgggggcta ggaagagctt tctctaggag gcggcgctc gggagcc	357				
atg gtg gac cgg ggc cct ctg ctc acc tcg gcc atc atc ttc tac ctg	405				
Met Val Asp Arg Gly Pro Leu Leu Thr Ser Ala Ile Ile Phe Tyr Leu		180	185	190	
1					
gcc atc ggg gcg gcg atc ttc gaa gtg ctg gag gag cca cac tgg aag	453				
Ala Ile Gly Ala Ala Ile Phe Glu Val Leu Glu Glu Pro His Trp Lys		195	200	205	
25					
gag gcc aag aaa aac tac tac aca cag aag ctg cat ctg ctc aag gag	501				
Glu Ala Lys Lys Asn Tyr Tyr Thr Gln Lys Leu His Leu Leu Lys Glu		210	215	220	
35					
ttc ccg tgc ctg ggt cag gag ggc ctg gac aag atc cta gag gtg gta	549				
Phe Pro Cys Leu Gly Gln Glu Gly Leu Asp Lys Ile Leu Glu Val Val		225	230	235	
50					
tct gat gct gca gga cag ggt gtc gcc atc aca ggg aac cag acc ttc	597				
Ser Asp Ala Ala Gly Gln Gly Val Ala Ile Thr Gly Asn Gln Thr Phe		245	250	255	
65					
aac aac tgg aac tgg ccc aat gca atg att ttt gca gcg acc gtc att	645				
35		260	265	270	



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ccc cgg aag gcc ctg cag gty aag ggg agc aca gcc tcc aag gtc 1221  
Ser Arg Lys Ala Leu Glu Val Lys Gly Ser Thr Ala Ser Lys Asp Val  
275 280 285  
aac atc ttc agc ttc ctt tcc aag aag gaa gag acc tac aac gac ctc 1269  
Asn Ile Phe Ser Phe Leu Ser Lys Lys Glu Glu Thr Tyr Asn Asp Leu  
290 295 300  
atc aag aag atc ggg aag aag gcc atg aag aca agc ggg ggt ggg gag 1317  
Ile Lys Glu Ile Gly Lys Lys Ala Met Lys Thr Ser Gly Gly Gly Glu  
305 310 315 320  
aag ggc cgg ggc cca ggg ctg ggg cct caa ggc ggt ggg ctc cca gca 1365  
Thr Gly Pro Gly Pro Gly Leu Gly Pro Glu Gly Gly Leu Pro Ala  
325 330 335  
ctg ccc cct tcc ctg gty ccc ctg gta gtc tac tcc aag aac cgg gty 1413  
Leu Pro Pro Ser Leu Val Pro Leu Val Val Tyr Ser Lys Asn Arg Val  
340 345 350  
ccc aac ttg gaa gag gty tca cag aca ctg aag agc aaa ggc caa gta 1461  
Pro Thr Leu Glu Glu Val Ser Glu Thr Leu Arg Ser Lys Ile His Val  
355 360 365  
tca aag tcc cca gat gag gag gct gty gaa cgg gcc cct gaa gac agc 1509  
Ser Arg Ser Pro Asp Glu Glu Ala Val Ala Arg Ala Pro Glu Asp Ser  
370 375 380  
tcc cct gcc ccc gag gty ttc atg aac cag ctg gac cgc atc agc gag 1557  
Ser Pro Ala Pro Glu Val Phe Met Asn Glu Leu Asp Arg Ile Ser Glu  
385 390 395 400  
gaa tgc gag cca tgg gac gcc cag gac tac cac cca ctc atc ttc cag 1605  
Glu Cys Glu Pro Trp Asp Ala Glu Asp Tyr His Pro Leu Ile Phe Glu  
405 410 415  
gac gcc agc atc acc ttc gty aac aag gag gct ggc ctc tca gac gag 1653  
Asp Ala Ser Ile Thr Phe Val Asn Thr Glu Ala Gly Leu Ser Asp Glu  
420 425 430  
gag acc tcc aag tcc tcc cta gag gac aac ttg gca ggg gag gag agc 1701  
Glu Thr Ser Lys Ser Ser Leu Glu Asp Asn Leu Ala Gly Glu Ser  
435 440 445  
ccc cag cag ggg gct gaa gcc aag gcc ccc ctg aac atg ggc gag ttc 1749  
Pro Glu Glu Gly Ala Glu Ala Lys Ala Pro Leu Asn Met Gly Glu Phe

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450 455 460  
ccc tcc tcc tcc gag tcc acc ttc acc agc act gag tct gag ctc tct 1797  
Pro Ser Ser Ser Glu Ser Thr Phe Thr Ser Thr Glu Ser Glu Leu Ser  
465 470 475 480  
gtg cct tac gaa cag ctg atg aat gag tac aac aag gct aac agc ccc 1845  
Val Pro Tyr Glu Glu Leu Met Asn Glu Tyr Asn Lys Ala Asn Ser Pro  
485 490 495  
aag ggc aca tgaagcagg ccgctccc aaccacact tgaagg 1890  
Lys Gly Thr  
10  
cccttccc cctcaccta ggtgtcccg agatgaccg gacgctggc cctgtgtgg 1950  
ggggagcct cgaactgg agtggggggc caggggact cctaacctt caccatccc 2010  
agctagatgt atgcacggga caggccctt gtccaccag tgaacatcac cctgtgctg 2070  
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ggacaggttg gcaagactga cccctggag cccctggctg cagggtcttt gtccacacat 2190  
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cccagagctg tgttccctgt ctcaagtlcaa gcaatggcag accgaaggt ttcctgggc 2610  
cccacagtg taggaggag agtagcagag catgggttac tggaaagcgg gactgttag 2670  
gctgtgtgac agggagctgc aagaatggag ctgaatctg gctgtgtctg cccctacccc 2730  
tccctgcgcg cggagaaactg caaacctgc ccgttggcc caggacctgc acctccatc 2790  
ctgtgtctt ctcccttcc gtgccttga ccaagacac actgcgcgc ttcctctcc 2850  
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ggcagaaact gctgtacta gacttctg gtctccatg atgttccacc tggggctggc 3150  
cnaatgtgc ctgaatgtt ttgttatct ttgtttatc tttaaacaa actgtgtt 3210  
ttatatcct ggaatctgt gtgtgttca gaggcagtg ttaagagca ggtgtccaa 3270  
gattggagga tctagtgt gtccctcgc ccgaacac atttggcct ttltgtgga 3330  
cctatccaa ggcacatgat tcaaggaca tgtccccag caggtgtgga gaaaggaca 3390

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gag gcc aaa gct gcc cga gcc cga gct ctg gaa agg gag tca ggg tcc 361  
 Glu Ala Lys Ala Ala Arg Ala Arg Ala Leu Ala Arg Ala Ser Gly Ser 105  
 95 100  
 taatctgga tgggtattga taatgtccaa cctgctggag ccccttcaca tgggtgatga 400  
 tgcceatga cctgttagaa attgaatcct gctcaaca ttgttgcoct tcttactaac 460  
 ctggaccgt gattgagccc aagaaaccag ggaactacgc atttggccaa tgcnaaaga 520  
 acagaacttt gcccaactga cacttctgt gtacaatgac tgaaccttt ctgttagttt 580  
 gtttcttgt ttgagagtg tgaatgcgac cgtggctttt ccaaaagttt ctgaacttgt 640  
 ggtttacccc ctcaaccttc caggagcga gttgttaca ggttagacgt ggcagctctg 700  
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 attctctgg 770

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 <211> 1229  
 <212> DNA  
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 <222> (36)...(554)

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 tgaagctgc atctgagaaa gtgcccaga agaca atg gac tat gtg tgc tgt 113  
 Met Asp Tyr Val Cys Cys  
 1 5

gct tac aac aac ata ecc ggc agg caa gat gaa act cat ttc aca gtt 161  
 Ala Tyr Asn Asn Ile Thr Gly Arg Gln Asp Glu Thr His Phe Thr Val  
 10 15 20  
 atc atc act tcc gta gga ctg gag aag ctt gca cag aaa gga aaa tca 209  
 Ile Ile Thr Ser Val Gly Leu Glu Lys Leu Ala Gln Lys Gly Lys Ser  
 25 30 35  
 ttg tca cct tta gca agt ata act gga ata tca cta ttt ttg att ata 257  
 Leu Ser Pro Leu Ala Ser Ile Thr Gly Ile Ser Leu Phe Leu Ile Ile  
 40 45 50  
 tcc atg tgt ctt ctc ttc cta tgg aaa aaa tat caa ccc tac aaa gtt 305

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ctgaggtgag caaagcagg aaggggcatc caactcgggt gaactggagg cgggcaggaa 3450  
 gcaatcatc agagcgtc agctcgttc actctctgcc ttctgcaca ctactctggg 3510  
 gcagtggggc cagagccac ctcccacaa tgtgaagaca gtgatggga cgtgccaca 3570  
 ccccacttc tctagcgtt tgcagagcc gcccccagc aggggctctga aaaggagcag 3630  
 cctcgtattt ttctgaaa tgttttaag aaccatgtt ttctgtgttg tccgtgcatc 3690  
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 caataaaca tgaggtgg 3768

<210> 89  
 <211> 770  
 <212> DNA  
 <213> Homo sapiens  
 <220>  
 <221> CDS  
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<400> 89  
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 Met Ala Ser Ser Gly Ala Gly Asp Pro Leu  
 1 5 10

gat tet aag cgt gga gag gcc ccg ttc gct cag cgt atc gac ccg act 101  
 Asp Ser Lys Arg Gly Glu Ala Pro Phe Ala Gln Arg Ile Asp Pro Thr  
 15 20 25

cgg gag aag ctg aca ccc gag caa ctg cat tcc atg cgg cag gcg gag 149  
 Arg Glu Lys Leu Thr Pro Glu Gln Leu His Ser Met Arg Gln Ala Glu  
 30 35 40

ctt gcc cag tgg cag aag gtc eta cca cgg cgg cga acc cgg aac atc 197  
 Leu Ala Gln Trp Gln Lys Val Leu Pro Arg Arg Thr Arg Asn Ile  
 45 50 55

gtg acc gcc eta gcc atc ggg gcc ctg gtg ttg gct att tat ggt tac 245  
 Val Thr Gly Leu Gly Ile Gly Ala Leu Val Leu Ala Ile Tyr Gly Tyr  
 60 65 70

acc ttc tac tct att tcc cag gag cgt ttc eta gat gag cta gaa gac 293  
 Thr Phe Tyr Ser Ile Ser Gln Glu Arg Phe Leu Asp Glu Leu Asp  
 75 80 85 90

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Ser Met Cys Leu Leu Phe Leu Thr Lys Lys Tyr Gln Pro Tyr Lys Val  
 55 60 65 70  
 ata aaa cag aaa cta gaa ggc agy cca gaa aca tac agy aaa gct 353  
 Ile Lys Gln Lys Leu Gln Gly Arg Pro Gln Thr Lys Tyr Arg Lys Ala  
 75 80 85  
 caa aca ttt cca ggc cat gaa gat gct ctg gat gac ttc gga ata cat 401  
 Gln Thr Phe Ser Gly His Gln Asp Ala Leu Asp Asp Phe Gly Ile Tyr  
 90 95 100  
 gaa ttt gtc gct ttt cca gat gtc tct gtc gtc tcc agy atc cca agc 449  
 Gln Phe Val Ala Phe Pro Asp Val Ser Gly Val Ser Arg Ile Pro Ser  
 105 110 115  
 agy tct gtc cca gcc tct gat tgt gta tcy ggg caa gat ttg cac agt 497  
 Arg Ser Val Pro Ala Ser Asp Cys Val Ser Gly Gln Asp Leu His Ser  
 120 125 130  
 aca gtc tat gaa gtc atc cag cac atc cct gcc cag cag caa gac cat 545  
 Thr Val Tyr Gln Val Ile Gln His Ile Pro Ala Gln Gln Asp His  
 135 140 145 150  
 cca gag tgaacttca tgggtcaaac agtcaactcg agtgaatttc tgaagaac 600  
 Pro Gln  
 20  
 atttaaggaa aaaaagctgg aaaaagtat taatctggaa tcaagtgaaga aaccaagacc 660  
 aacacctctt acatcatatc cctttacag cagatatagag gcatttatgc aaattgaact 720  
 gaaggtttt cagcatatac acaatgctt gtgcacaga aaaaatggtt ggggaatat 780  
 tctcagctgg agagtcgttc tcaatctgac ggggagagag aagaatgacg ggggttcctc 840  
 ataagtttg tatgaatat ctctacaac ctcaattagt tctactctac aatttcaacta 900  
 tcatcaaac tgaagatac ctgtctaac tacaatgctg gaaacttacc atgtctcgat 960  
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 ttatttcca aatttctac ttgttatctg taacacaaag taattagat ggtttccaca 1080  
 aaaaacaaac tatgcctctc ctcttttttc aatcacagct agtatcttg agagagctg 1140  
 tgaacactta aggaatgac tactaaagc ttattttat ttttttaag gaagatgga 1200  
 ttcaaataaa ttattctgtt ttgtgtttt 1229  
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WO 00/05367 PCT/JP99/03929  
 100/177  
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 Ile Gly Ala Val Ile Ala Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val  
 20 25 30  
 Pro Arg Ser Ala Ser Ile Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu  
 35 40 45  
 Ala Leu Gln Leu His Pro Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln  
 50 55 60  
 Gln Lys Phe Gln Asp Leu Gly Ala Ala Tyr Gln Val Leu Ser Asp Ser  
 65 70 75 80  
 Gln Lys Arg Lys Gln Tyr Asp Thr Tyr Gly Gln Gln Gly Leu Lys Asp  
 85 90 95  
 Gly His Gln Ser Ser His Gly Asp Ile Phe Ser His Phe Phe Gly Asp  
 100 105 110  
 Phe Gly Phe Met Phe Gly Gly Thr Pro Arg Gln Gln Asp Asn Ile  
 115 120 125  
 Pro Arg Gly Ser Asp Ile Ile Val Asp Leu Gln Val Thr Leu Gln Gln  
 130 135 140  
 Val Tyr Ala Gly Asn Phe Val Gln Val Val Arg Asn Lys Pro Val Ala  
 145 150 155 160  
 Arg Gln Ala Pro Gly Lys Arg Lys Cys Asn Cys Arg Gln Gln Met Arg  
 165 170 175  
 Thr Thr Gln Leu Gly Pro Gly Arg Phe Gln Met Thr Gln Gln Val Val  
 180 185 190  
 Cys Asp Gln Cys Pro Asn Val Lys Leu Val Asn Gln Gln Arg Thr Leu  
 195 200 205  
 Gln Val Gln Ile Gln Pro Gly Val Arg Asp Gly Met Gln Tyr Pro Phe  
 210 215 220  
 Ile Gly Gln Gly Gln Pro His Val Asp Gly Gln Pro Gly Asp Leu Arg  
 225 230 235 240  
 Phe Arg Ile Lys Val Val Lys His Pro Ile Phe Gln Arg Arg Gly Asp  
 245 250 255  
 35

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Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile Tyr Pro Asn Ser  
115 120 125  
Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe Pro Tyr Arg Asp  
130 135 140  
5 Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu Ile Ile Leu Leu  
145 150 155 160  
Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu Ile Ser Cys Val  
165 170 175  
Tyr Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser Ser Asp Val Leu  
180 185 190  
10 Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu Pro Tyr Asp  
195 200 205  
Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro Pro Tyr Val  
210 215 220  
15 Ser Ala  
225  
<210> 93  
<211> 195  
20 <212> PRT  
<213> Homo sapience  
  
<400> 93  
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Ser Glu Ala Ser Ala Asn Leu Gly Gly Val Pro Ser Lys Arg Leu Lys  
20 25 30  
Met Gln Tyr Ala Thr Gly Pro Leu Leu Lys Phe Gln Ile Cys Val Ser  
35 40 45  
30 Xaa Gly Tyr Arg Arg Val Phe Glu Glu Tyr Met Arg Val Ile Ser Gln  
50 55 60  
Arg Tyr Pro Asp Ile Arg Ile Glu Gly Glu Asn Tyr Leu Pro Gln Pro  
65 70 75 80  
Ile Tyr Arg His Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu  
85 90 95

Asp Leu Tyr Thr Asn Val Thr Ile Ser Leu Val Glu Ser Leu Val Gly  
260 265 270  
Phe Glu Met Asp Ile Thr His Leu Asp Gly His Lys Val His Ile Ser  
275 280 285  
5 Arg Asp Lys Ile Thr Arg Pro Gly Ala Lys Leu Trp Lys Lys Gly Glu  
290 295 300  
Gly Leu Pro Asn Phe Asp Asn Asn Ile Lys Gly Ser Leu Ile Ile  
305 310 315 320  
Thr Phe Asp Val Asp Phe Pro Lys Glu Gln Leu Thr Glu Ala Arg  
325 330 335  
10 Glu Gly Ile Lys Gln Leu Leu Lys Gln Gly Ser Val Gln Lys Val Tyr  
340 345 350  
Asn Gly Leu Gln Gly Tyr  
355  
15 <210> 92  
<211> 226  
<212> PRT  
20 <213> Homo sapience  
  
<400> 92  
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1 5 10 15  
Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu Gly Val Trp Tyr  
20 25 30  
Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu Ser Ala Leu Ala  
35 40 45  
Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu Gly Gly Asp Phe  
50 55 60  
30 Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile Ala Ile Ser Leu  
65 70 75 80  
Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly Ala Tyr Lys Gln  
85 90 95  
Arg Ala Ala Trp Ile Ile Pro Phe Phe Cys Tyr Gln Ile Phe Asp Phe  
100 105 110

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Ile Gly Leu Ile Ile Val Gly Lys Asp Pro Phe Ala Phe Phe Gly Met  
100 105 110  
Gln Ala Pro Ser Ile Trp Gln Trp Gly Gln Glu Asn Lys Val Tyr Ala  
115 120 125  
5 Cys Met Met Val Phe Phe Leu Ser Asn Met Ile Glu Asn Gln Cys Met  
130 135 140  
Ser Thr Gly Ala Phe Glu Ile Thr Leu Asn Asp Val Pro Val Trp Ser  
145 150 155 160  
Lys Leu Glu Ser Gly His Leu Pro Ser Met Gln Gln Leu Val Gln Ile  
165 170 175  
10 Leu Asp Asn Glu Met Lys Leu Asn Val His Met Asp Ser Ile Pro His  
180 185 190  
His Arg Ser  
195  
15 <210> 94  
<211> 339  
<212> PRT  
<213> Homo sapience  
20 <400> 94  
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Leu Leu Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu  
20 25 30  
25 Thr Leu Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu  
35 40 45  
Thr Asp Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu  
50 55 60  
30 Glu Leu Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser  
65 70 75 80  
Ala Arg Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu  
85 90 95  
Asn Gly Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu  
100 105 110

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Thr Asp Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu  
115 120 125  
Phe Gly Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg  
130 135 140  
5 Ser Leu Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu  
145 150 155 160  
Leu Asn Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His  
165 170 175  
Met Ile Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu  
180 185 190  
10 Gly Ile Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His  
195 200 205  
Ala Leu Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr  
210 215 220  
15 Pro Gly Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn  
225 230 235 240  
Ile Val Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn  
245 250 255  
Asn Gly Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu  
260 265 270  
20 Met Leu Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu  
275 280 285  
Gln Pro Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp  
290 295 300  
25 Ala Trp Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe  
305 310 315 320  
Lys Ser Gly Val Asp Ala Asp Ser Ser Tyr Phe Lys Ile Phe Lys Thr  
325 330 335  
Lys His Asp  
30 <210> 95  
<211> 487  
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<213> Homo sapience  
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<400> 95  
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 Pro Gly Glu Leu Gly Leu Pro His Pro Leu Ser Thr Gly Gly Leu Pro  
 20 25 30  
 Val Ala Ser Glu Asp Gly Ala Leu Arg Ala Pro Glu Ser Gln Ser Val  
 35 40 45  
 Thr Pro Lys Pro Leu Glu Thr Glu Pro Ser Arg Glu Thr Ala Trp Ser  
 50 55 60  
 Ile Gly Leu Gln Val Thr Val Pro Phe Met Phe Ala Gly Leu Gly Leu  
 65 70 75 80  
 Ser Trp Ala Gly Met Leu Leu Asp Tyr Phe Gln His Trp Pro Val Phe  
 85 90 95  
 Val Glu Val Lys Asp Leu Leu Thr Leu Val Pro Pro Leu Val Gly Leu  
 100 105 110  
 Lys Gly Asn Leu Glu Met Thr Leu Ala Ser Arg Leu Ser Thr Ala Ala  
 115 120 125  
 Asn Thr Gly Gln Ile Asp Asp Pro Gln Glu Gln His Arg Val Ile Ser  
 130 135 140  
 Ser Asn Leu Ala Leu Ile Gln Val Gln Ala Thr Val Val Gly Leu Leu  
 145 150 155 160  
 Ala Ala Val Ala Ala Leu Leu Gly Val Val Ser Arg Glu Glu Val  
 165 170 175  
 Asp Val Ala Lys Val Glu Leu Leu Cys Ala Ser Ser Val Leu Thr Ala  
 180 185 190  
 Phe Leu Ala Ala Phe Ala Leu Gly Val Leu Met Val Cys Ile Val Ile  
 195 200 205  
 Gly Ala Arg Lys Leu Gly Val Asn Pro Asp Asn Ile Ala Thr Pro Ile  
 210 215 220  
 Ala Ala Ser Leu Gly Asp Leu Ile Thr Leu Ser Ile Leu Ala Leu Val  
 225 230 235 240  
 Ser Ser Phe Phe Tyr Arg His Lys Asp Ser Arg Tyr Leu Thr Pro Leu  
 245 250 255  
 Val Cys Leu Ser Phe Ala Ala Leu Thr Pro Val Trp Val Leu Ile Ala  
 260 265 270  
 35

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Lys Gln Ser Pro Pro Ile Val Lys Ile Leu Lys Phe Gly Trp Phe Pro  
 275 280 285  
 Ile Ile Leu Ala Met Val Ile Ser Ser Phe Gly Gly Leu Ile Leu Ser  
 290 295 300  
 5 Lys Thr Val Ser Lys Gln Gln Tyr Lys Gly Met Ala Ile Phe Thr Pro  
 305 310 315 320  
 Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg  
 325 330 335  
 Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu  
 340 345 350  
 Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser  
 355 360 365  
 Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Val Val Pro  
 370 375 380  
 15 Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser  
 385 390 395 400  
 Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu  
 405 410 415  
 Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu  
 420 425 430  
 Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu  
 435 440 445  
 Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe  
 450 455 460  
 25 Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Gly Ile Ser  
 465 470 475 480  
 Glu Leu Ala Ser Gly Pro Pro  
 485  
 30 <210> 96  
 <211> 393  
 <212> PRT  
 <213> Homo sapience  
 35 <400> 96

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Met Arg Thr Leu Phe Asn Leu Leu Trp Leu Ala Ala Cys Ser Pro  
1 5 10 15  
Val His Thr Thr Leu Ser Lys Ser Asp Ala Lys Lys Ala Ala Ser Lys  
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6 Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp Lys Pro Val Gln Asp Arg  
35 40 45  
Gly Leu Val Val Thr Asp Leu Lys Ala Glu Ser Val Val Leu Glu His  
50 55 60  
Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp Arg His Phe Ala Gly Asp  
10 65 70 75 80  
Val Leu Gly Tyr Val Thr Pro Trp Asn Ser His Gly Tyr Asp Val Thr  
85 90 95  
Lys Val Phe Gly Ser Lys Phe Thr Gln Ile Ser Pro Val Trp Leu Gln  
100 105 110  
15 Leu Lys Arg Arg Gly Arg Glu Met Phe Glu Val Thr Gly Leu His Asp  
115 120 125  
Val Asp Gln Gly Trp Met Arg Ala Val Arg Lys His Ala Lys Gly Leu  
130 135 140  
His Ile Val Pro Arg Leu Leu Phe Glu Asp Trp Thr Tyr Asp Asp Phe  
20 145 150 155 160  
Arg Asn Val Leu Asp Ser Glu Asp Glu Ile Glu Glu Leu Ser Lys Thr  
165 170 175  
Val Val Gln Val Ala Lys Asn Gln His Phe Asp Gly Phe Val Val Glu  
180 185 190  
25 Val Trp Asn Gln Leu Leu Ser Gln Lys Arg Val Gly Leu Ile His Met  
195 200 205  
Leu Thr His Leu Ala Glu Ala Leu His Gln Ala Arg Leu Leu Ala Leu  
210 215 220  
Leu Val Ile Pro Pro Ala Ile Thr Pro Gly Thr Asp Gln Leu Gly Met  
30 225 230 235 240  
Phe Thr His Lys Glu Phe Glu Gln Leu Ala Pro Val Leu Asp Gly Phe  
245 250 255  
Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala His Gln Pro Gly Pro Asn  
260 265 270  
35 Ala Pro Leu Ser Trp Val Arg Ala Cys Val Gln Val Leu Asp Pro Lys

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275 280 285  
Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly Leu Asn Phe Tyr Gly Met  
290 295 300  
Asp Tyr Ala Thr Ser Lys Asp Ala Arg Glu Pro Val Val Gly Ala Arg  
6 305 310 315 320  
Tyr Ile Gln Thr Leu Lys Asp His Arg Pro Arg Met Val Trp Asp Ser  
325 330 335  
Gln Ala Ser Glu His Phe Phe Glu Tyr Lys Lys Ser Arg Ser Gly Arg  
340 345 350  
10 His Val Val Phe Tyr Pro Thr Leu Lys Ser Leu Gln Val Arg Leu Glu  
355 360 365  
Leu Ala Arg Glu Leu Gly Val Val Ser Ile Trp Glu Leu Gly Gln  
370 375 380  
Gly Leu Asp Tyr Phe Tyr Asp Leu Leu  
15 385 390  
210> 97  
211> 196  
212> PRT  
213> Homo sapience  
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Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Thr Leu Ala  
20 25 30  
Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro Gly Gly  
35 40 45  
Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His His Ile Thr Gly  
30 50 55 60  
Leu Arg Val Ser Val Gly Leu Leu Leu Val Lys Ser Val Gln Val Lys  
65 70 75 80  
Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly Asn Thr  
85 90 95  
35 Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val Phe Val

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100 105 110  
Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser Lys Asp  
115 120 125  
Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser Ala Tyr  
130 135 140  
Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gln Tyr Gln  
145 150 155 160  
Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro Leu Glu  
165 170 175  
10 Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala Asn Ser  
180 185 190  
Pro Val Gly Arg  
195

15 <210> 98  
<211> 107  
<212> PRT  
<213> Homo sapiens

20 <400> 98  
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Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly Ile  
35 40 45  
Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys Ser  
50 55 60  
Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val Ala  
65 70 75 80  
Ala Glu Gly Phe Val Val Gly Ala Met Thr Val Gly Met Gly Tyr Ser  
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Met Tyr Arg Glu Phe Trp Ala Lys Pro Lys Pro  
100 105

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<210> 99  
<211> 350  
<212> PRT  
<213> Homo sapiens

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20 25 30  
Arg Ser Ser Gly Gly Gly Trp Ala Asp Pro Arg Thr Cys Leu Ser  
35 40 45  
Leu Leu Ser Leu Gly Thr Cys Leu Gly Leu Ala Trp Phe Val Phe Gln  
50 55 60  
15 Gln Ser Glu Lys Phe Ala Lys Val Glu Asn Gln Tyr Gln Leu Lys  
65 70 75 80  
Leu Glu Thr Asn Glu Phe Gln Gln Leu Gln Ser Lys Ile Ser Leu Ile  
85 90 95  
Ser Glu Lys Trp Gln Lys Ser Glu Ala Ile Met Glu Gln Leu Lys Ser  
100 105 110  
Phe Gln Ile Ile Ala His Leu Lys Arg Leu Gln Glu Ile Asn Glu  
115 120 125  
Val Lys Thr Trp Ser Asn Arg Ile Thr Glu Lys Gln Asp Ile Leu Asn  
130 135 140  
25 Asn Ser Leu Thr Thr Leu Ser Gln Asp Ile Thr Lys Val Asp Gln Ser  
145 150 155 160  
Thr Thr Ser Met Ala Lys Asp Val Gly Leu Lys Ile Thr Ser Val Lys  
165 170 175  
Thr Asp Ile Arg Arg Ile Ser Gly Leu Val Thr Asp Val Ile Ser Leu  
180 185 190  
30 Thr Asp Ser Val Gln Glu Leu Glu Asn Lys Ile Glu Lys Val Glu Lys  
195 200 205  
Asn Thr Val Lys Asn Ile Gly Asp Leu Leu Ser Ser Ile Asp Arg  
210 215 220  
35 Thr Ala Thr Leu Arg Lys Thr Ala Ser Glu Asn Ser Gln Arg Ile Asn



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225 230 235 240  
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245 250 255  
Thr Asp Arg Phe Leu Ser Leu Gln Gly Asp Arg Ala Lys Val Leu Lys  
260 265 270  
Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys Val Tyr Asn Leu Lys  
275 280 285  
Lys Asp Phe Ser Arg Leu Leu Gln Pro Leu Val Asn Asp Leu Thr Leu Arg  
290 295 300  
Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg Gln Lys Gln Ile Ala  
305 310 315 320  
Phe Leu Ser Gln Lys Ile Ser Asn Leu Thr Ile Val Gln Ala Gln Ile  
325 330 335  
Lys Asp Ile Lys Asp Gln Ile Ala His Ile Ser Asp Met Asn  
340 345 350  
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20 25 30  
Ile Val Gly Ser Ser His Gln Leu Gly Phe Trp Phe Ser His Leu Gln  
35 40 45  
Ser Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Gln Cys Val  
50 55 60  
Asn Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu  
65 70 75 80  
Leu Val Val Gly Gln Ala Pro Ala Trp Gln Gly Ser Leu Leu Arg Gly  
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35 Arg Pro Ala Gly Ala His Leu Cys Ala Ala

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<211> 1074  
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<213> Homo Sapiens  
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attaaaaag cctataggaa actagccctg cagcttcatc ccgaccgaa cccatgatgat  
cccaaaagcc aggaagaatt ccaagatctg ggtgtgtct atgaggtctc gtccagatagt  
gagaaagaga aacagtagca taatttgt gaagaagatc taaaagatgag tcatcagagc  
tcccatgag agaatcttc acaattctt ggggattctg gtccatgctc tggaggaacc  
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aattgacaaa tctcattagt tgnrtacatg gtgtgcttgg agatggatat taactacatg  
gatgtcaca agttacatat ttcccgatc agatcacca ggcagagagc gaagctatgg  
aagaagaagg aaggctccc caacttgac aacacaata tcaaggctc ttgttaatc  
actttgatg tggatttcc aagaagacag ttaagaagg aagcagaga aggtatcaaa  
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<213> Homo Sapiens  
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120  
35

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5  
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actgtgta ttatccaaa ctccattcag gaatacatc ggcacatgcc tctaatttt 420  
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<213> Homo Sapience

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gttattagcc agcggtaacc agacatccgc attgaaggag agaatcact cctcaacca 240  
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attgttgca aggtaccttt tgcctttctt ggcataagc cctcagcat ctggcagtgg 360  
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<211> 1017  
<212> DNA  
<213> Homo Sapience

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ggaaatgttg aggaatgggc ttaccagttg tctaaactag ggtttctct tgtgtgtca 240  
ggcagagag tgcattgact ggaaggggtg aaaaagaagt gctcagaga ttggaattta 300  
aagaaaaag atactctgt ttgcccctt gacctgacag acactggttc ccatgaagcg 360  
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accgctggt ccataggct taagtgacc gtgccttca tgttgccgg cctggagctg 240  
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gaactttga catgtgtgc gccctggtg ggcctgaagg ggaactgga gatgacactg 360  
gcatacagc tctccagc tgcaacact ggacaattg atgaoccca ggaagcagc 420  
agagtcatca gcagcaacct ggcctcacc caggtcagg ccactgctgt ggggctcttg 480  
gctgtgtgg ctgcgtgtt gttggcggtg gtgtctcag aggaatgga tctgccag 540  
gtggagtgc tgtgtccag cagtgtctc actgcttcc ttgacctt tgcctgggg 600  
gtgtgatgg tctgtatgt gattgtgt cgaagctcg ggtcaacc agacaactt 660  
ggcagccca ttgagccag cctgggagac ctcaacac tgccttctt ggtttggtt 720

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agaagatcttc tctaaagaca caaagataagt cgttatctga cgcgcgtgt ctgcacaga	780
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atccgaagt ttgtctgtgt cccatcatc ctgcacatg tcatagaaag ttccgtgaga	900
ctatcttga gcaaacctgt tcttaaacag cagtataaag gcatgtgagt attaacccg	960
gtcatgtgt gtgtgtgtgt caatctgtgt gcatcaca ccaagcgaat ctcaactac	1020
ctgcacatgt ggaagtgcac tgcgtctgt cccctcaga tgaagaatt ctggccaac	1080
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gaactgtcat ctgtacttc c	1461
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<211> 1179	
<212> DNA	
<213> Homo Sapiens	
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tcaagataagc cgtgtgaaga ccgtgtgtgt gtgtgtgacg aactcaaaag tgaagatgt	180
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tcaatccaga caatgaagga ccaagggccc cgtatgtgtt ggtgaagcca ggcctcaag	1020
caattcttc agtacaagaa gaaacgcagt ggtgaagcag tgccttcta ccaaacctg	1080
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<213> Homo Sapiens	
<400> 107	
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cgtgcagag ccaatctgtt gctgtcaag ctgtccccc tgggtgtgccc caactgtgga	120
gggaagatgt atgtaccctgt aggaagcaag tatttcaga ccaatgaaga ctacagacat	180
gaatcaaggt ggtctgtgt gtctgtagt ctctctctgt tgaagaagt ccaagttgaa	240
cttgaagact cctgtgaagt gaaactgtga gcaatgtgt ggaatccaa ggaagtgaac	300
ctgcagcag gcaatcatc caaaagtc ttgtctgct tcaagatt cctccgtgtt	360
atgtcatgt acaacagcaa ggaacgtat tctattttg ggaacttga tggcaagatc	420
tccctgtct acccaagcaa agaaaggtgac gtgtgtgtgt gcatctatga caagtatca	480
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gaagcaacag ttaactaac atactaaga aactcaaccg tgggtgc	588
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<400> 108	
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gaacatttg taaccgttga aataagcgtt ttgcagaa ctgttcat tgaatttat	180
aaactgaaga gcaagtgaaa tactaaatg tcaatcata tgaacaaat ggtgtgtgca	240
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		ctagaaccca atgacttcca acaacttcaa agtaaatca gtttaatttc agaaaagtgg	300		1	
		cagaactcy aagctatcat ggaacnatty aagtcctttc aataattgc tcatctaaag	360		5	
	<400> 109	cgtctacagg aagaattaa tgaggtaaa acttggtcca ataggataac tgaanaacag	420		age acc ttt tgc ctg ctg cta tac etc atc ggg gcg gtg att gcc	223
15		gatatactga acacagctct gcgcagctt tctcangca ttacaaaagt agaccaagt	480	15	Ser Thr Phe Cys Leu Leu Leu Tyr Leu Ile Gly Ala Val Ile Ala	271
		acnaactcca tggcaaaaga tgttggctc agattacca gtgtaaaac agatatacga	540		gga cga gat ttc tat aag atc ttg ggg gtg cct cga agt gcc tot ata	
		cggatttcag gtttagtaac tgatgata tontgacay attctgtgca agaatagaa	600		Gly Arg Asp Phe Tyr Lys Ile Leu Gly Val Pro Arg Ser Ala Ser Ile	319
		aataaataag agaaagtag aaaaataca aaaaataca gtaaaaata taggtgatct tctttcaagc	660		Lys Asp Ile Lys Lys Ala Tyr Arg Lys Leu Ala Leu Gln Leu His Pro	367
20		agttatgac gaacagcaac gctccgaag acagatcty anaattaca aagaattaac	720		gac cgg aac cct gat gat cca cca gcc cag gag aca ttc cag gat ctg	415
		tctgttaaga agacgttaac cgaactaaag agtgaactcy acaacatac agatagattt	780		Asp Arg Asn Pro Asp Asp Pro Gln Ala Gln Glu Lys Phe Gln Asp Leu	463
		ctaagcttag aagtgacag agccaagtt ctgaagacag tgacttttgc aaatgatcta	840		ggg gct get tat gag gtt ctg tca gat agt gag aca cgg aaa cag tac	
		aaaccaagg tgtataatct aagaaggac ttttccggt tagaaccatt agtaaatgat	900		Gly Ala Ala Tyr Glu Val Leu Ser Asp Ser Glu Lys Arg Lys Gln Tyr	
		ttaacactac gcattggggg attggtacc gacttactac aagagagaga agaaattgct	960		gat act tat ggt gaa gaa gga tta aca gat ggt cat cag agc tcc cat	
25		ttcttaagtg aaaaatac taatttaaca atagttccag ctgagattaa ggtattaaa	1020		Asp Thr Tyr Gly Glu Glu Gly Leu Lys Asp Gly His Gln Ser Ser His	
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	ggcaggccaa gcttctatg taacagttag cacagtatag tggatcac acatacgtg				75	
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90 95 100  
gga gac att ttt tca cac ttc ttt ggg gat ttt ggt ttc atg ttt gga 511  
gly asp ile phe ser his phe phe gly asp phe gly phe met phe gly  
105 110 115  
gga acc cct cgt cag caa gac aga aat att cca aga gga agt gat att 559  
gly thr pro arg gln gln asp arg asn ile pro arg gly ser asp ile  
120 125 130  
att gta gat cta gaa gta act ttg gaa gaa gta tat gca gga aat ttt 607  
ile val asp leu glu val thr leu glu glu val tyr ala gly asn phe  
135 140 145 150  
gtg gaa gta gtt aga aac aac cct gtc gca agg cag gct cct ggc aaa 655  
val glu val val arg asn lys pro val ala arg gln ala pro gly lys  
155 160 165  
cgg aag tgc aat tgt cgg caa gag atg cgg acc acc cag ctg ggc cct 703  
arg lys cys asn cys arg gln gln met arg thr thr gln leu gly pro  
170 175 180  
ggg cgc ttc caa atg acc cag gag gtc gtc tgc gac gaa tgc cct aat 751  
gly arg phe gln met thr gln glu val val cys asp glu cys pro asn  
185 190 195  
gtc aaa cta ttg aat gaa gaa cga aag ctg gaa gta gaa ata gag cct 799  
val lys leu val asn glu glu arg thr leu glu val ile glu pro  
200 205 210  
ggg gtc aga gac ggc atg gag tac ccc ttt att gga gaa ggt gag cct 847  
gly val arg asp gly met glu tyr pro phe ile gly glu gly pro  
215 220 225 230  
cac ttg gat ggg gag cct gga gat tta cgg ttc cga atc aaa gtt gtc 895  
his val asp gly glu pro gly asp leu arg phe arg ile lys val val  
235 240 245  
aag caa cca ata ttt gaa agg aga gga gat gat ttg tac aca aat gtc 943  
lys his pro ile phe glu arg arg gly asp asp leu tyr thr asn val  
250 255 260  
aca atc tca tta gtc gag tca ctg gtc ggc ttt gag atg gat att act 991  
thr ile ser leu val glu ser leu val gly phe glu met asp ile thr  
265 270 275  
cac ttg gat ggt cac aag gta cat att tcc cgg gat aag atc acc agg 1039

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his leu asp gly his lys val his ile ser arg asp lys ile thr arg  
280 285 290  
cca gga ggc aag cta tgg aag aaa ggg gaa ggg ctg ccc aac ttt gac 1087  
pro gly ala lys leu thr lys lys gly glu gly leu pro asn phe asp  
295 300 305 310  
aac aac aat atc aag ggc tct ttg ata atc aat ttt gat ttg gat ttt 1135  
asn asn asn ile lys gly ser leu ile ile thr phe asp val asp phe  
315 320 325  
cca aaa gaa cag tta aca gag gaa ggc aga gaa ggt atc aac cag cta 1183  
pro lys glu gln leu thr glu glu ala arg glu gly ile lys gln leu  
330 335 340  
ctg aaa caa ggg tca gtc cag aag gta tac aat gga ctg caa gga tat 1231  
leu lys gln gly ser val gln lys val tyr asn gly leu gln gly tyr  
345 350 355  
tgagagaga ataaatttg accttggtta aaataagaga ataaagata ttatuaatc 1290  
gcaaggttt ttgtgtgtg ttgtgttt tattttaac atgaagata ggttaattt 1350  
ttttatctaa tgatatacat gaatagaata agagagctta agaatgtc cattgaact 1410  
cggaaagaa tgacacagaa aaggtttact aataactcc ccttgaggga tttaagtct 1470  
gtgtgtccg cctgaatttc aagaattaa gctgaagag gactccagga gcaaaagaa 1530  
cacatataag aggttgtag ttgttagaa tttaatcaa aatgaact ggaagagctc 1590  
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gcggcgcaac gggcgagcgg gccgggggc ggaagcgscg aggaagcggc agcagcgscg 180  
cggcgggcgc caggcgagcg gtcgagcgt cctgaanaat tgcgagcgcg ctccgagcac 240

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tgcgcgcgga gcg atg aag atg gtc gcg ccc tgg acg cgg ttc tac tcc 289  
 Met Lys Met Val Ala Pro Trp Thr Arg Phe Tyr Ser  
 1 5 10  
 aac agc tgc tgc tgc tgc cat gtc cgc acc ggc acc atc ctg ctc 337  
 Asn Ser Cys Cys Leu Cys Cys His Val Arg Thr Gly Thr Ile Leu Leu  
 15 20 25  
 ggc gtc tgg tat ctg atc atc aat gct gtg gta ctg ttg att tta ttg 385  
 Gly Val Trp Tyr Leu Ile Ile Asn Ala Val Val Leu Leu Ile Leu Leu  
 30 35 40  
 10 agt gcc ctg gct gat ccg gat cag tat aac ttt tca agt tct gaa ctg 433  
 Ser Ala Leu Ala Asp Pro Asp Gln Tyr Asn Phe Ser Ser Ser Glu Leu  
 45 50 55 60  
 gga ggt gac ttt gag ttc atg gat gat gcc aac atg tgc att gcc att 481  
 Gly Gly Asp Phe Glu Phe Met Asp Asp Ala Asn Met Cys Ile Ala Ile  
 65 70 75  
 15 gcg att tct ctt ctc atc ctg ata tgt gct atg gct act tac gga 529  
 Ala Ile Ser Leu Leu Met Ile Leu Ile Cys Ala Met Ala Thr Tyr Gly  
 80 85 90  
 gcg tac aag caa cgc gca gcc tgg atc atc cca ttc ttc tgt tac cag 577  
 Ala Tyr Lys Gln Arg Ala Ala Trp Ile Ile Pro Phe Cys Tyr Gln  
 95 100 105  
 atc ttt gac ttt gcc ctg aac atg ttg gtt gca atc act gtc ctt att 625  
 Ile Phe Asp Phe Ala Leu Asn Met Leu Val Ala Ile Thr Val Leu Ile  
 110 115 120  
 25 tat cca aac tcc att cag gaa tac ata cgg caa ctg cct cct aat ttt 673  
 Tyr Pro Asn Ser Ile Gln Glu Tyr Ile Arg Gln Leu Pro Pro Asn Phe  
 125 130 135 140  
 ccc tac aga gat gat gtc atg tea tgc aat cct acc tgt ttg gtc ctt 721  
 Pro Tyr Arg Asp Asp Val Met Ser Val Asn Pro Thr Cys Leu Val Leu  
 145 150 155  
 30 att att ctt ctg ttt att agc att atc ttg act ttt aag ggt tac ttg 769  
 Ile Ile Leu Leu Phe Ile Ser Ile Ile Leu Thr Phe Lys Gly Tyr Leu  
 160 165 170  
 att agc tgt gtt tgg aac tgc tac cga tac atc aat ggt agg aac tcc 817  
 Ile Ser Cys Val Trp Asn Cys Tyr Arg Tyr Ile Asn Gly Arg Asn Ser

175 180 185  
 tct gat gtc ctg gtt tat gtt acc agc aat gac act acg gtc cta 865  
 Ser Asp Val Leu Val Tyr Val Thr Ser Asn Asp Thr Thr Val Leu Leu  
 190 195 200  
 5 ccc ccg tat gat gat gcc act gtg aat ggt gct gcc aag gag cca ccg 913  
 Pro Pro Tyr Asp Asp Ala Thr Val Asn Gly Ala Ala Lys Glu Pro Pro  
 205 210 215 220  
 cca cct tac gtg tct gcc taagcttcca agtgggggga gctggggg 960  
 Pro Pro Tyr Val Ser Ala  
 225  
 10 agcagctga ctttgcagac atctgacaa tagttctggtt atttcacatt tgcctagcgc 1020  
 ctctctagc ttgtttgttg ctgaatgct actttttaaa atttagatgt tagattgaaa 1080  
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 aaaaagggtt tctttcctt gcaagctaca tcaactgct ttgaacttcc aagtatgct 1860  
 agtcacattt taatatgtaa acattttcag aaaaatgagg attgacctcc ttgtatgac 1920  
 tttttacott gactacctga attgcaagg atttttatat attcatatgt tacaagtca 1980  
 gcaactctcc tgttggttca ttatgaatg tctgtaaat taagtgttt gcaattaaa 2040  
 caaggttgc ccaac 2054

&lt;210&gt; 113

&lt;211&gt; 1380

&lt;212&gt; DNA

&lt;213&gt; Homo Sapience

&lt;220&gt;

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<400> 113  
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Met Arg Leu Leu  
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ctg ctt ctc cta gtc gcg tct gcg atg gtc cgg agc gag tgc tgc  
Leu Leu Leu Leu Val Ala Ala Ser Ala Met Val Arg Ser Gln Ala Ser  
5 10 15 20  
gac aat ctg ggc ggc ggc ccc agc aag aga tta aag atg cag tac ggc  
Ala Asn Leu Gln Gln Val Pro Ser Lys Arg Leu Lys Met Gln Tyr Ala  
25 30 35  
aag ggg cag ctg cto aag ttc cag att tgt gtc tcc tga ggt tat aag  
Thr Gln Pro Leu Leu Lys Phe Gln Ile Cys Val Ser Xaa Gln Tyr Arg  
40 45 50  
cgg gtc ttt gag gag tac atg cgg gtc att agc cag cgg tac cca gac  
Arg Val Phe Gln Gln Tyr Met Arg Val Ile Ser Gln Arg Tyr Pro Asp  
55 60 65  
atc cgc att gaa gga gag aat tac ctc cct cca cca ata tat aga cac  
Ile Arg Ile Gln Gln Gln Asn Tyr Leu Leu Pro Ile Tyr Arg His  
70 75 80  
ata gca tct ttc ctg tca gtc ttc aca cta gta tta ata ggc tta ata  
Ile Ala Ser Phe Leu Ser Val Phe Lys Leu Val Leu Ile Gln Leu Ile  
85 90 95 100  
aatt gtc ggc aag gat cct ttt gct ttc ttc ggc atg caa gct cct agc  
Ile Val Gln Lys Asp Pro Phe Ala Phe Phe Gln Met Gln Ala Pro Ser  
105 110 115  
atc tgg cag tgg ggc caa gaa aat aag gtc tat gca tgt atg atg gtc  
Ile Trp Gln Trp Gln Gln Gln Asn Lys Val Tyr Ala Cys Met Met Val  
120 125 130  
ttc ttc ttg agc aac atg att gag aac cag tgt atg tca aca ggt gca  
Phe Phe Leu Ser Asn Met Ile Gln Asn Gln Cys Met Ser Thr Gln Ala  
135 140 145  
ttc gag ata aat tta aat gat gta cct gtc tgg tct aag ctg gaa tct  
534

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Phe Gln Ile Thr Leu Asn Asp Val Pro Val Trp Ser Lys Leu Gln Ser  
150 155 160  
ggt cac ctt cca tcc atg caa caa ctt gtc caa att ctt gac aat gaa  
Gln His Leu Pro Ser Met Gln Gln Leu Val Gln Ile Leu Asp Asn Gln  
165 170 175 180  
atg aag ctc aat gtc cat atg gat tca atc cca ccc cat cga tca  
Met Lys Leu Asn Val His Met Asp Ser Ile Pro His His Arg Ser  
185 190 195  
tag caaccactat cagcactgaa aactctttg catbaagga tcaatgaa  
agaagcgtga ctgaactat gaagcctgt actgaagca gcaagctgtt agtaagacc  
agaatcttc ttggaagct cgttgaact ctggaanac ctcaatgcaa gatagtgtt  
cagtcgtgga atatttga atctgaca tcaatgagt gcaataaac tgaatagct  
tcccacccc ccacaaatc accaaptaa tgtgtgtgt tgtttttt ttbaagtaa  
acaattactac ttgtaacttt tttaactagt catatttga aagtaagaaa attgaattac  
aatitgattt ttltccaaa gatgtctgt aatctgtt tgcatttala tgaatattg  
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cagatgaag attatgggg aatccata ttcaagrac tcaataat ttgtgtatg  
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atctgtgagt taagtgtca tgccttgacc aatcaatgaa atgattaat taactgggc  
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gaactgtgt cgggcgtct tctccccc gaactgggtg tggcgtgag ca atg aac  
Met Asn  
1

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5 tgg gag ctg ctg tgg ctg ctg tgc ggc ctg ctg ctg ctg 166  
 Trp Glu Leu Leu Leu Trp Leu Leu Val Leu Cys Ala Leu Leu Leu Leu  
 5 10 15  
 ttg gtc cag ctg ctg cgc ttc ctg agg gct gac ggc ctg acg cta 214  
 Leu Val Gln Leu Leu Arg Phe Leu Arg Ala Asp Gly Asp Leu Thr Leu  
 20 25 30  
 cta tgg gcc gag tgg cag gga cga cgc cca gaa tgg gag ctg act gat 262  
 Leu Trp Ala Glu Trp Gln Gly Arg Arg Pro Glu Trp Glu Leu Thr Asp  
 35 40 45 50  
 atg gtc gtc tgg gtc act gga gcc tcg agt gga att ggt gag gag ctg 310  
 Met Val Val Trp Val Thr Gly Ala Ser Ser Gly Ile Gly Glu Glu Leu  
 55 60 65  
 gct tac cag ttc tct aaa cta gga gtt tct ctg ctg tca gcc aga 358  
 Ala Tyr Gln Leu Ser Lys Leu Gly Val Ser Leu Val Leu Ser Ala Arg  
 70 75 80  
 aga gtc cat gag ctg gaa agg gtc aaa aga aga tgc cta gag aat ggc 406  
 Arg Val His Glu Leu Glu Arg Val Lys Arg Arg Cys Leu Glu Asn Gly  
 85 90 95  
 aat tta aaa gaa aat ata ctt gtt ttg ccc ctt gac ctg acc gac 454  
 Asn Leu Lys Glu Lys Asp Ile Leu Val Leu Pro Leu Asp Leu Thr Asp  
 100 105 110  
 act ggt tcc cat gaa gcg gct acc aaa gct gtt ctc cag gag ttt ggt 502  
 Thr Gly Ser His Glu Ala Ala Thr Lys Ala Val Leu Gln Glu Phe Gly  
 115 120 125 130  
 aga atc gac att ctg gtc aac aat ggt gga atg tcc cag cgt tct ctg 550  
 Arg Ile Asp Ile Leu Val Asn Asn Gly Gly Met Ser Gln Arg Ser Leu  
 135 140 145  
 tgc atg gat acc agc ttg gat gtc tac aga aag cta ata gag ctt aac 598  
 Cys Met Asp Thr Ser Leu Asp Val Tyr Arg Lys Leu Ile Glu Leu Asn  
 150 155 160  
 tcc tta ggg acg gtc tcc ttg aca aaa tgc gtt ctg cct cac atg atc 646  
 Tyr Leu Gly Thr Val Ser Leu Thr Lys Cys Val Leu Pro His Met Ile  
 165 170 175  
 gag agg aag caa gga aag att gtt act gtc aat agc atc ctg ggt atc 694  
 Glu Arg Lys Gln Gly Lys Ile Val Thr Val Asn Ser Ile Leu Gly Ile

180 185 190  
 ata tct gta cct ctt tcc att gga tac tgt gct agc aag cat gct ctc 742  
 Ile Ser Val Pro Leu Ser Ile Gly Tyr Cys Ala Ser Lys His Ala Leu  
 195 200 205 210  
 cgg ggt ttt ttt aat ggc ctt cga aca gaa ctt gcc aca tac cca ggt 790  
 Arg Gly Phe Phe Asn Gly Leu Arg Thr Glu Leu Ala Thr Tyr Pro Gly  
 215 220 225  
 ata ata gtt tct aac att tgc cca gga cct gtc caa tca aat att gtc 838  
 Ile Ile Val Ser Asn Ile Cys Pro Gly Pro Val Gln Ser Asn Ile Val  
 230 235 240  
 gag aat tcc cta gct gga gaa gtc aca aag act ata gcc aat aat gga 886  
 Glu Asn Ser Leu Ala Gly Glu Val Thr Lys Thr Ile Gly Asn Asn Gly  
 245 250 255  
 gac cag tcc cac aag atg aca acc agt cgt tgt gtc cgg ctg atg tta 934  
 Asp Gln Ser His Lys Met Thr Thr Ser Arg Cys Val Arg Leu Met Leu  
 260 265 270  
 atc agc atg gcc aat gat ttg aaa gaa gtt ttg atc tca gaa caa cct 982  
 Ile Ser Met Ala Asn Asp Leu Lys Glu Val Trp Ile Ser Glu Gln Pro  
 275 280 285 290  
 ttc ttg tta gta aca tat ttg tgg caa tac atg cca acc tgg gcc tgg 1030  
 Phe Leu Leu Val Thr Tyr Leu Trp Gln Tyr Met Pro Thr Trp Ala Trp  
 295 300 305  
 tgg ata acc aac aag atg ggg aag aaa agg att gag aac ttt aag agt 1078  
 Trp Ile Thr Asn Lys Met Gly Lys Lys Arg Ile Glu Asn Phe Lys Ser  
 310 315 320  
 ggt gtc gat gca gac tct tct tat ttt aaa atc ttt aag aca aaa cat 1126  
 Gly Val Asp Ala Asp Ser Tyr Phe Lys Ile Phe Lys Thr Lys His  
 325 330 335  
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 Asp  
 30  
 35 <210> 115





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Val Ile Cys Gly Val Gly Gly Asn Leu Val Ala Ile Gln Thr Ser Arg  
325 330 335  
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Ile Ser Thr Tyr Leu His Met Trp Ser Ala Pro Gly Val Leu Pro Leu  
340 345 350  
cag atg aag aaa ttc tgg ccc aac ccc tgt tet act ttc tgc acg tca 1159  
Gln Met Lys Lys Phe Trp Pro Asn Pro Cys Ser Thr Phe Cys Thr Ser  
355 360 365  
gaa atc aat tcc atg tca gct cga gtc ctg etc ttg ctg gtc gtc cca 1207  
Glu Ile Asn Ser Met Ser Ala Arg Val Leu Leu Leu Val Val Pro  
370 375 380  
ggc cat ctg att ttc ttc tac atc atc tac ctg gtc gag ggt cag tca 1255  
Gly His Leu Ile Phe Phe Tyr Ile Ile Tyr Leu Val Glu Gly Gln Ser  
385 390 395 400  
gtc ata aac agc cag acc ttt gtc gtc etc tac ctg ctg gca ggc ctg 1303  
Val Ile Asn Ser Gln Thr Phe Val Val Leu Tyr Leu Leu Ala Gly Leu  
405 410 415  
atc cag gtc aca atc ctg ctg tac ctg gca gaa gtc atg gtt cgg ctg 1351  
Ile Gln Val Thr Ile Leu Leu Tyr Leu Ala Glu Val Met Val Arg Leu  
420 425 430  
act tgg cac cag ggc ctg gat cct gac aac cag tgc atc ccc tac ctt 1399  
Thr Trp His Gln Ala Leu Asp Pro Asp Asn His Cys Ile Pro Tyr Leu  
435 440 445  
aca ggg ctg ggg gac ctg etc ggt act ggc etc ctg gca etc tgc ttt 1447  
Thr Gly Leu Gly Asp Leu Leu Gly Thr Gly Leu Leu Ala Leu Cys Phe  
450 455 460  
ttc act gac tgg cta ctg aag agc aag gca gag ctg ggt ggc atc tca 1495  
Phe Thr Asp Trp Leu Leu Lys Ser Lys Ala Glu Leu Gly Ile Ser  
465 470 475 480  
gaa ctg gca tct gga cct ccc taactgggccc ccgctgtccc catitgtcca ttac 1550  
Glu Leu Ala Ser Gly Pro Pro  
485  
aatttctct cacatcagtg ggaacagaa ttcagtttct cccctgccc gtccttggga 1610  
tgttgacccc ctgcctctgc agtagccttt tgtgagtcg ctaaggctgc tctcacac 1670  
ctcggtctg ggttgatac ctgagctgc aatagagccc tgaatcaag agcatggtt 1730

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tcttttctg tcccaagcct cagaactctt gagctgtggc ttaactgtg tcttcaaccag 1970  
gttcaagctc cgtgggccc actgtctgtg tgcacagag gttacagcc tcccagcat 2030  
ggggcctcat acacaccttc atctgacctc aacatttaac cgtgtccttg ctgtcttttt 2090  
atttctctt ttgttagcaa aaacctctat tttagtttca ataatacagag aagtgtaaaa 2150  
taaacagat tatattgt 2168  
  
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cctactgtga cacacctaac atg cgg aca etc ttc aac etc etc tgg ctt 110  
Met Arg Thr Leu Phe Asn Leu Leu Trp Leu  
1 5 10  
gcc ctg gcc tgc agc cct gtt cac act acc ctg tca aag tca gat gcc 158  
Ala Leu Ala Cys Ser Pro Val His Thr Thr Leu Ser Lys Ser Asp Ala  
15 20 25  
aaa aaa gcc gcc tca aag acg ctg ctg gag aag agt cag ttt tca gat 203  
Lys Lys Ala Ala Ser Lys Thr Leu Leu Glu Lys Ser Gln Phe Ser Asp  
30 35 40  
aag ccg gtc cna gac cgg ggt ttg gtc gtc acg gac etc aaa gct gag 254  
Lys Pro Val Gln Asp Arg Gly Leu Val Val Thr Asp Leu Lys Ala Glu  
45 50 55  
agt gtc gtt ctt gag cat cgc agc tac tgc tgc gca aag gcc cgg gac 302  
Ser Val Val Leu Glu His Arg Ser Tyr Cys Ser Ala Lys Ala Arg Asp  
60 65 70  
aga cac ttt gct ggg gat gta ctg ggc tat gtc act cca tgg aac agc 350

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Arg His Phe Ala Gly Asp Val Leu Gly Tyr Val Thr Pro Trp Asn Ser  
75 80 85 90  
cat gag tac gat gtc acc aag gtc ttt ggg agc aag ttc aca cag atc  
His Gly Tyr Asp Val Thr Lys Val Phe Gly Ser Lys Phe Thr Gln Ile  
5 95 100 105  
tca ccc gtc tgg ctg cag ctg aag aga cgt ggc cgt gag atg ttt gag  
Ser Pro Val Trp Leu Gln Leu Lys Arg Arg Gly Arg Gln Met Phe Gln  
110 115 120  
gtc aag ggc ctg ccc gac gtc gac caa ggg tgg atg cga gct gtc aag  
Val Thr Gly Leu His Asp Val Asp Gln Gly Trp Met Arg Ala Val Arg  
125 130 135  
aag cat ggc aag ggc ctg ccc ata gtc cct cgg ctg ctg ttt gag gac  
Lys His Ala Lys Gly Leu His Ile Val Pro Arg Leu Leu Phe Gln Asp  
140 145 150  
tgg act tac gat gat ttc cgg aac gtc tta gac agt gag gat gag ata  
Trp Thr Tyr Asp Asp Phe Arg Asn Val Leu Asp Ser Gln Asp Gln Ile  
155 160 165 170  
gag gag ctg agc aag aac gtc gtc cag gtc gca aag aac cag cat ttc  
Gln Gln Leu Ser Lys Thr Val Val Gln Val Ala Lys Asn Gln His Phe  
175 180 185  
gat ggc ttc gtc gtc gag gtc tgg aac cag ctg cta agc cag aag cgc  
Asp Gly Phe Val Val Gln Val Trp Asn Gln Leu Leu Ser Gln Lys Arg  
190 195 200  
gtg ggc ctg atc ccc atg ctg acc ccc ttg ggc gag gct ctg ccc cag  
Val Gly Leu Ile His Met Leu Thr His Leu Ala Gln Ala Leu His Gln  
205 210 215  
ggc cgg ctg ctg ggc ctg ctg gtc atc ccg cct ggc atc acc ccc ggg  
Ala Arg Leu Leu Ala Leu Leu Val Ile Pro Pro Ala Ile Thr Pro Gly  
220 225 230  
acc gac cag ctg gtc atg ttc aag ccc aag gag ttc gag cag ctg ggc  
Thr Asp Gln Leu Gly Met Phe Thr His Lys Gln Phe Gln Gln Leu Ala  
235 240 245 250  
ccc gtc ctg gat gat ttc agc ctg atg acc tac gac tac ttc aca ggc  
Pro Val Leu Asp Gly Phe Ser Leu Met Thr Tyr Asp Tyr Ser Thr Ala  
255 260 265

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cat cag cct ggc cct aat gca ccc ctg tcc tgg gtc cga ggc tgc gtc  
His Gln Pro Gly Pro Asn Ala Pro Leu Ser Trp Val Arg Ala Cys Val  
270 275 280  
cag gtc ctg gac ccg aag tcc aag tgg cga agc aaa atc ctg ggg  
Gln Val Leu Asp Pro Lys Ser Lys Trp Arg Ser Lys Ile Leu Leu Gly  
285 290 295  
ctc aac ttc tac gat atg gac tac ggc acc tcc aag gat ggc cgt gag  
Leu Asn Phe Tyr Gly Met Asp Tyr Ala Thr Ser Lys Asp Ala Arg Gln  
300 305 310  
cct gtc gtc ggg ggc aag tac atc cag aca ctg aag gac ccc ccc  
Pro Val Val Gly Ala Arg Tyr Ile Gln Thr Leu Lys Asp His Arg Pro  
315 320 325 330  
cgg atg gtc tgg gag agc agc cag ggc tca gag ccc ttc ttc gag tac aag  
Arg Met Val Trp Asp Ser Gln Ala Ser Gln His Phe Phe Gln Tyr Lys  
335 340 345  
aag agc cgc agt ggg aag ccc gtc gtc ttc tac cca acc ctg aag tcc  
Lys Ser Arg Ser Gly Arg His Val Val Phe Tyr Pro Thr Leu Lys Ser  
350 355 360  
ctg cag gtc cgg ctg gag ctg ggc cgg gag ctg ggc gtc ggg gtc tct  
Leu Gln Val Arg Leu Leu Gln Leu Ala Arg Gln Leu Gly Val Val Ser  
365 370 375  
atc tgg gag ctg ggc cag ggc ctg gac tac ttc tac gac ctg ctg t  
Ile Trp Gln Leu Gly Gln Gly Leu Asp Tyr Phe Tyr Asp Leu Leu  
380 385 390  
aggtggagcat tgcggcctcc gcggtggagc tgcctcttcc taagccatgg agtgagtgag  
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<222> (8)...(598)

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&lt;400&gt; 117

aaagcg atg tgg agg gtg ccc gcc aca ace aga cgc cca gtc aca gcc  
Met Trp Arg Val Pro Gly Thr Thr Arg Arg Pro Val Thr Gly

49

1 5 10

gag agc cct ggg atg cac cgg cca gag gcc atg ctg ctg ctg etc acg  
Glu Ser Pro Gly Met His Arg Pro Glu Ala Met Leu Leu Leu Thr

97

15

ctt gcc etc ctg ggg gcc ccc acc tgg gca ggg aag atg tat ggc cct  
Leu Ala Leu Leu Gly Gly Pro Thr Trp Ala Gly Lys Met Tyr Gly Pro

145

35 40 45

gga gga gcc aag tat ttc agc acc act gaa gac tac gac cat gaa atc  
Gly Gly Lys Tyr Phe Ser Thr Thr Glu Asp Tyr Asp His Glu Ile

193

50 55 60

aca ggg ctg cgg gtg tct gta ggt ctt etc ctg gtg aaa agt gtc cag  
Thr Gly Leu Arg Val Ser Val Gly Leu Leu Val Lys Ser Val Gln

241

65 70 75

gtg aaa ctt gga gac tcc tgg gac gtg aaa ctg gga gcc tta ggt ggg  
Val Lys Leu Gly Asp Ser Trp Asp Val Lys Leu Gly Ala Leu Gly Gly

289

80 85 90

aat acc cag gaa gtc acc ctg cag cca ggc gaa tac atc aca aaa gtc  
Asn Thr Gln Glu Val Thr Leu Gln Pro Gly Glu Tyr Ile Thr Lys Val

337

95 100 105 110

ttt gtc gcc ttc caa gct ttc etc cgg ggt atg gtc atg tac acc agc  
Phe Val Ala Phe Gln Ala Phe Leu Arg Gly Met Val Met Tyr Thr Ser

385

115 120 125

aag gac cgc tat ttc tat ttt ggg aag ctt gat ggc cag atc tcc tct  
Lys Asp Arg Tyr Phe Tyr Phe Gly Lys Leu Asp Gly Gln Ile Ser Ser

433

130 135 140

gcc tac ccc agc caa gag ggg cag gtg ctg ggc atc tat ggc cag  
Ala Tyr Pro Ser Gln Glu Gly Gln Val Leu Val Gly Ile Tyr Gly Gln

481

145 150 155

tat caa etc ctt ggc atc aag agc att ggc ttt gaa tgg aat tat cca  
Tyr Gln Leu Leu Gly Ile Lys Ser Ile Gly Phe Glu Trp Asn Tyr Pro

529

160 165 170

cta gag gag ccg acc act gag cca cca gtt aat etc cta tac tca gca  
cga

577

Leu Glu Glu Pro Thr Thr Glu Pro Pro Val Asn Leu Thr Tyr Ser Ala  
175 180 185 .190

aac tca ccc gtg ggt cgc taggtgggg tatggggcca tccgagctga ggcca  
Asn Ser Pro Val Gly Arg

630

195

tctgtgggt ggtgctgat ggtactggag taactgagtc gggacgtga atctgaatcc  
accaataaat aaagctcttg c

690

711

&lt;210&gt; 118

&lt;211&gt; 651

&lt;212&gt; DNA

&lt;213&gt; Homo Sapiens

&lt;220&gt;

&lt;221&gt; CDS

&lt;222&gt; (242)....(565)

15

&lt;400&gt; 118

aaagaacaa gccgggggac tgcagaccag ggaactgggc cgcggggcgg gaagaagtcgg  
ggcagcgtt gccagggccg aaaggaacttt ggggtgggg gctgggagtc cgtgtctga

60

120

180

240

286

g atg gag cag aag ctt gtg gag gag att ctt caa gca atc act atg  
Met Glu Gln Lys Leu Val Glu Glu Ile Leu Gln Ala Ile Thr Met

1 5 10 15

334

tca aca gac aca ggt gtt tcc ctt cct tca tat gag gaa gat cag gga  
Ser Thr Asp Thr Gly Val Ser Leu Pro Ser Tyr Glu Glu Asp Gln Gly

25

20 25 30

tca aaa etc att cga aaa gct aaa gag gca cca ttc gta ccc gtt gga  
Ser Lys Leu Ile Arg Lys Ala Lys Glu Ala Pro Phe Val Pro Val Gly

382

35 40 45

ata ggg ggt ttt gca gca att gtt gca tat gga tta tat aaa ctg aag  
Ile Ala Gly Phe Ala Ala Ile Val Ala Tyr Gly Leu Tyr Lys Leu Lys

430

50 55 60

agc agg gga aat act aaa atg tcc att cat ctg atc cag atg cgt gtc  
Ser Arg Gly Asn Thr Lys Met Ser Ile His Leu Ile His Met Arg Val

35

478

65 70 75  
gca gcc caa gcc ttt gtt gta gga gca atg act ggt atg ggc tat 526  
ala ala gln gly phe val val gly ala met thr val gly met gly tyr  
80 85 90 95  
tcc atg tat cgg gaa ttc tgg gca aaa cct aag cct tagaagaa 570  
ser met tyr arg glu phe trp ala lys pro lys pro  
100 105  
ggagatgcctg cctggcctcg ctggagagac tgccttagt tagatgctt attactaag  
ttacctatta ttgttgaaa t 630  
651  
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tccctggctc tccagac atg tct gag gty aag agc cgg aag tgg ggg 110  
met ser glu val lys ser arg lys lys ser gly  
1 5 10  
ccc aag gga gcc cct gct gcg gag ccc ggg aag cgg agc gag ggc ggg 158  
pro lys gly ala pro ala ala glu pro gly lys arg ser glu gly gly  
15 20 25  
aag aac ccc gtc gcc cgg agc agc gga gcc ggg ggc tgg gca gac ccc 206  
lys thr pro val ala arg ser ser gly gly gly trp ala asp pro  
30 35 40  
cga acg tgc ctg agc ctg ctg tgg ggg agc tgc ctg ggc ctg gcc 254  
arg thr cys leu ser leu leu ser leu gly thr cys leu gly leu ala  
45 50 55  
tgg ttc gta ttc cag cag tca gaa aaa ttc gca aag gtc gaa aac caa 302  
trp phe val phe gln gln ser glu lys phe ala lys val glu asn gln  
60 65 70 75

tac cag tta ctg aac cta gaa acc aat gaa ttc cca caa ctt caa agt 350  
tyr gln leu leu lys leu glu thr asn glu phe gln gln leu ser  
80 85 90  
aaa acc agt tta att tca gaa aag tgg cag aaa tct gaa gct atc atg 398  
lys ile ser leu ile ser glu lys trp gln lys ser glu ala ile met  
95 100 105  
gaa caa tgg aag tct ttt caa ata att gct cat cta aag cgt cta cag 446  
glu gln leu lys ser phe gln ile ile ala his leu lys arg leu gln  
110 115 120  
gaa gaa att aat gag gta aaa act tgg tcc aat agg ata act gaa aaa 494  
glu glu ile asn glu val lys thr trp ser asn arg ile thr glu lys  
125 130 135  
cag gat ata ctg aac aac agt ctg acg acg ctt tct caa gac att aca 542  
gln asp ile leu asn asn ser leu thr thr leu ser gln asp ile thr  
140 145 150 155  
aaa gta gac caa agt aca act tcc atg gca aaa gat gtt ggt ctc aag 590  
lys val asp gln ser thr thr ser met ala lys asp val gly leu lys  
160 165 170  
att aca agt gta aaa aca gat ata cga cgg att tca ggt tta gta act 638  
ile thr ser val lys thr asp ile arg arg ile ser gly leu val thr  
175 180 185  
gat gta ata tca tgg aca gat tct gtc caa gaa cta gaa aat aac ata 686  
asp val ile ser leu thr asp ser val gln glu leu leu asn lys ile  
190 195 200  
gag aaa gta gaa aaa aat aca gta aaa aat ata ggt gat ctt tca 724  
glu lys val glu lys asn thr val lys asn ile gly asp leu leu ser  
205 210 215  
agc agt att gat cga aca gca acg ctg cga aag aca gaa tct gaa aat 782  
ser ser ile asp arg thr ala thr leu arg lys thr ala ser glu asn  
220 225 230 235  
tca caa aga att aac tct gtt aag aag acg cta acc gaa cta aag agt 830  
ser gln arg ile asn ser val lys lys thr leu thr glu leu lys ser  
240 245 250  
gac ttc gac aac cat aca gat aga ttt cta agc tta gaa ggt gac aga 878  
asp phe asp lys his thr asp arg phe leu ser leu glu gly asp arg 36

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255 260 265  
gcc aag gtt ctg aag aca gtg act ttt gca aat gat cta aca cca aag 926  
Ala Lys Val Leu Lys Thr Val Thr Phe Ala Asn Asp Leu Lys Pro Lys  
270 275 280  
5 gtc tat aat cta aag aag gac ttt tcc cgt tta gaa cca tta gta aat 974  
Val Tyr Asn Leu Lys Lys Asp Phe Ser Arg Leu Glu Pro Leu Val Asn  
285 290 295  
gat tta aca cta cgc att ggg aga ttg gtt acc gac tta cta cca aga 1022  
Asp Leu Thr Leu Arg Ile Gly Arg Leu Val Thr Asp Leu Leu Gln Arg  
300 305 310 315  
10 gag aag aag att gct ttc tta aat gaa aca ata tct aat tta aca ata 1070  
Glu Lys Glu Ile Ala Phe Leu Ser Glu Lys Ile Ser Asn Leu Thr Ile  
320 325 330  
gtc aca gct gag att aag gat att aag gat gaa ata gca ccc att tca 1118  
Val Gln Ala Glu Ile Lys Asp Ile Lys Asp Glu Ile Ala His Ile Ser  
335 340 345  
15 gat atg aat tagttgaca ttattgagat tagactaagg taatttttt aat 1170  
Asp Met Asn  
350  
20 gggacctctc atgagaagac tagtaaatca aaataatga tattttgag caaaatcat 1230  
tttatattta atctatttt gtacagtaaa aataaaactt taacaacagt tgattttoca 1290  
aaataaatat gctaaaacct 1310  
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aacacagctg gtatttaag tctctggga cctactcag gaatgatccc cctcagtag 180

235 aagcagcagg tgatctaac tcccttcaaa gacagagcct gtcctgggaag cc atg  
Met  
1  
283 tcc tca gca ggc aca gca acc cct ctg gaa atg gat cac aca ctc act  
Ser Ser Ala Gly Thr Ala Thr Pro Leu Glu Met Asp His Lys Leu Thr  
5 10 15  
tct cag cca ggc agc cca agc ttc tat tgt aac agt agc ctc agt ata  
Ser Gln Pro Gly Arg Pro Ser Phe Tyr Cys Asn Ser Arg His Ser Ile  
20 25 30  
10 gtc gga tca tca cat cag ctg ggt ttt tgg ttt agt cat cta gag tgg  
Val Gly Ser Ser His Gln Leu Gly Phe Thr Phe Ser His Leu Glu Ser  
35 40 45  
tct gga cta aag gtc ttt cag gtc tcc ttg ccc tgt gag tgc gtc aac  
Ser Gly Leu Lys Val Phe Gln Val Ser Leu Pro Cys Glu Cys Val Asn  
50 55 60 65  
ctc ccc acc cga att gcc tca gtt gtc ctg agc ctc atg tct ctc ctg  
Leu Pro Thr Arg Ile Ala Ser Val Val Leu Ser Leu Met Ser Leu Leu  
70 75 80  
523 gtc gtc ggc cag gcc cct gca tgg gaa ggg agc ctg ctg ggc agg  
Val Val Gly Gln Ala Pro Ala Thr Glu Gly Ser Leu Leu Arg Gly Arg  
85 90 95  
cca gct ggg ggt gct ccc cta tgc gca gca tgaagtatt gaaggac  
Pro Ala Gly Gly Ala His Leu Cys Ala Ala  
100 105  
25 tggttgtta tggtgtgag cgtatcttc atggcagcg cgaagtggc caggtcagcc 630  
aggtcctgac agcctctct ctcggacttg tctctctg cccagggacc gtggagaag 690  
tgtcaggggc cgtctatcgc agcagcctgc tctctgacct tccctggcag tggtctggg 750  
gtggattccc tacaactaga tggtcaaggc ctacttttc ctcacacaaa ggaagtgcag 810  
ccacgtatgc tctgacttgc caactgaca aagtcaagt agcaggtcta ggcagaagact 870  
gggcaattga gcagagagga cggacctgtg agctgacca cgaaggcggac cctctacct 930  
tggtgggccc tggtcctggt ccttaggttt tgctaggttg tccctgttg gactcctaa 990  
ctaggtgata agcactggag ggggatgacc cgccttgacc gtgtttcttt aacctatcc 1050  
atataatagg gccgtgggat ggtgtatag gtaaaagagg atgatggtgt tttaagacca 1110  
gggtctggga cccgggtccc taacataat ttctctcct ggtatgctga caaaggtcta 1170  
aattagctta acaaaagac aggtgcctcgt cagccagagt tctgaaggcc atgcttttag 1230

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tttcctctgt tgcacattgc tctccagttc ctatgaaagc aacagagcct agggggcctg 1290  
gcaacagaaac aaaaacatct taaggctcagc ctgtgaagag cagggggttg tgcgtctgtc 1350  
ctgtctctct gcttcgcgaac ctcttcgaat aaacctact tctatttat 1400

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<212> PRT  
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1 5 10 15  
Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Asp Ile Val  
20 25 30  
Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu Asp  
15 35 40 45  
Ser Val Thr Glu Ser Pro Gln Arg Val Ile Ile Thr Glu Asp Asp Glu  
50 55 60  
Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu Gly  
20 65 70 75 80  
Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu Pro  
85 90 95  
Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr Ser  
100 105 110  
Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala His  
115 120 125  
Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val Thr  
130 135 140  
Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys Asn  
145 150 155 160  
Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu Glu  
165 170 175  
Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala Thr  
180 185 190  
Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu Trp

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195 200 205  
Cys Ser Gly Arg Val Cys Cys Glu Gly Met Leu Ile Gln Leu Arg Phe  
210 215 220  
Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg Pro  
5 225 230 235 240  
Val Ser Asp Gln Val Gln Ile Lys Val Thr Met Asn Asp Glu Asp Met  
245 250 255  
Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg Leu  
260 265 270  
Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro Lys  
10 275 280 285  
Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Ser Leu Ala Ile Leu Ser Glu  
290 295 300  
Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His Phe  
15 305 310 315 320  
Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp Gln  
325 330 335  
Phe Ser Gly Pro Lys Ile Met Gln Glu Gly Gln Pro Leu Lys Leu  
340 345 350  
Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly Ser  
20 355 360 365  
Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met Asn  
370 375 380  
Met Val Ile Tyr Ser Ile Asp Lys Ala Lys Lys Phe Arg Leu Asn Arg  
25 385 390 395 400  
Glu Gly Lys Gln Lys Ala Asp Lys Asn Arg Ala Arg Val Glu Glu Asn  
405 410 415  
Phe Leu Lys Leu Thr His Val Gln Arg Gln Glu Ala Ala Gln Ser Arg  
420 425 430  
Arg Glu Glu Lys Lys Arg Ala Glu Lys Glu Arg Ile Met Asn Glu Glu  
30 435 440 445  
Asp Pro Glu Lys Gln Arg Arg Leu Glu Glu Ala Ala Leu Arg Arg Glu  
450 455 460  
Gln Lys Lys Leu Glu Lys Lys Gln Met Lys Met Lys Gln Ile Lys Val  
35 465 470 475 480

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Lys Ala Met  
210 215 220  
Ser Phe Gly Glu Asn Asp Leu Phe Asp Gln Ile Pro Asn Ser Ser Gly  
225 230 235 240  
Ser Trp Leu Arg Tyr Ile Gln Asn Arg Leu Gln Lys Ile Met Gly Ile  
245 250 255  
Ser Leu Pro Leu Phe His Gly Arg Gly Val Phe Gln Tyr Ser Phe Gly  
260 265 270  
Leu Ile Pro Tyr Arg Arg Pro Ile Thr Thr Val Val Gly Lys Pro Ile  
275 280 285  
Glu Val Gln Lys Thr Leu His Pro Ser Glu Glu Val Asn Gln Leu  
290 295 300  
His Gln Arg Tyr Ile Lys Glu Leu Cys Asn Leu Phe Glu Ala His Lys  
305 310 315 320  
Leu Lys Phe Asn Ile Pro Ala Asp Gln His Leu Glu Phe Cys  
325 330  
15  
<210> 123  
<211> 267  
<212> PRT  
<213> Homo sapiens  
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<400> 123  
Met Ala Pro Trp Ala Leu Leu Ser Pro Gly Val Leu Val Arg Thr Gly  
1 5 10 15  
His Thr Val Leu Thr Trp Gly Ile Thr Leu Val Leu Phe Leu His Asp  
20 25 30  
Thr Glu Leu Arg Gln Trp Glu Gln Gly Glu Leu Leu Leu Pro Leu  
35 40 45  
Thr Phe Leu Leu Val Leu Gly Ser Leu Leu Leu Tyr Leu Ala Val  
50 55 60  
Ser Leu Met Asp Pro Gly Tyr Val Asn Val Gln Pro Gln Pro Gln Glu  
65 70 75 80  
Glu Leu Lys Glu Gln Thr Ala Met Val Pro Pro Ala Ile Pro Leu  
85 90 95  
35 Arg Arg Cys Arg Tyr Cys Leu Val Leu Gln Pro Leu Arg Ala Arg His

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Lys Ala Met  
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<211> 334  
<212> PRT  
<213> Homo sapiens  
5  
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1 5 10 15  
Thr Leu Ala Val Leu Gln Phe Val Phe Ser Phe Leu Ala Leu Ala Glu  
20 25 30  
Ile Cys Thr Val Gly Phe Ile Ala Leu Leu Phe Thr Arg Phe Trp Leu  
35 40 45  
Leu Thr Val Leu Tyr Ala Ala Trp Trp Tyr Leu Asp Arg Asp Lys Pro  
50 55 60  
Arg Gln Gly Gly Arg His Ile Gln Ala Ile Arg Cys Trp Thr Ile Trp  
65 70 75 80  
Lys Tyr Met Lys Asp Tyr Phe Pro Ile Ser Leu Val Lys Thr Ala Glu  
85 90 95  
Leu Asp Pro Ser Arg Asn Tyr Ile Ala Gly Phe His Pro His Gly Val  
100 105 110  
Leu Ala Val Gly Ala Phe Ala Asn Leu Cys Thr Glu Ser Thr Gly Phe  
115 120 125  
Ser Ser Ile Phe Pro Gly Ile Arg Pro His Leu Met Met Leu Thr Leu  
130 135 140  
Trp Phe Arg Ala Pro Phe Phe Arg Asp Tyr Ile Met Ser Ala Gly Leu  
145 150 155 160  
Val Thr Ser Glu Lys Glu Ser Ala Ala His Ile Leu Asn Arg Lys Gly  
165 170 175  
Gly Gly Asn Leu Leu Gly Ile Ile Val Gly Gly Ala Gln Glu Ala Leu  
180 185 190  
Asp Ala Arg Pro Gly Ser Phe Thr Thr Leu Leu Arg Asn Arg Lys Gly  
195 200 205  
Phe Val Arg Leu Ala Leu Thr His Gly Ala Pro Leu Val Pro Ile Phe



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100 105 110  
Cys Arg Gln Cys Arg Arg Cys Val Arg Arg Tyr Asp His His Cys Pro  
115 120 125  
Trp Met Gln Asn Cys Val Gly Gln Arg Asn His Pro Leu Phe Val Val  
130 135 140  
Tyr Leu Ala Leu Gln Leu Val Val Leu Leu Trp Gly Leu Tyr Leu Ala  
145 150 155 160  
Trp Ser Gly Leu Arg Phe Phe Gln Pro Trp Gly Leu Trp Leu Arg Ser  
165 170 175  
10 Ser Gly Leu Leu Phe Ala Thr Phe Leu Leu Ser Leu Phe Ser Leu  
180 185 190  
Val Ala Ser Leu Leu Leu Val Ser His Leu Tyr Leu Val Ala Ser Asn  
195 200 205  
15 Thr Thr Thr Trp Gln Phe Ile Ser Ser His Arg Ile Ala Tyr Leu Arg  
210 215 220  
Gln Arg Pro Ser Asn Pro Phe Asp Arg Gly Leu Thr Arg Asn Leu Ala  
225 230 235 240  
His Phe Phe Cys Gly Trp Pro Ser Gly Ser Trp Gln Thr Leu Trp Ala  
245 250 255  
20 Gln Gln Gln Gln Gln Gly Ser Ser Pro Ala Val  
260 265

<210> 124  
<211> 106  
<212> PRT  
<213> Homo sapience

<400> 124  
Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro Asn Lys Val Leu  
1 5 10 15  
Arg Tyr Lys Pro Pro Pro Ser Gln Cys Asn Pro Ala Leu Asp Asp Pro  
20 25 30  
Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe Ser Met Cys Gly  
35 40 45  
35 Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala Val Tyr Cys Ser

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50 55 60  
Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Gln Asp Thr Lys Gln Met  
65 70 75 80  
Met Ser Ser Phe Met Leu Ser Ile Ser Ala Val Val Met Ser Tyr Leu  
85 90 95  
5 Gln Asn Pro Gln Pro Met Thr Pro Pro Trp  
100 105

<210> 125  
<211> 224  
<212> PRT  
<213> Homo sapience

<400> 125  
Met Thr Leu Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro  
1 5 10 15  
Tyr Phe Ile Thr Tyr Lys Cys Ser Gly Leu Ser Gln Tyr Asn Ala Phe  
20 25 30  
Trp Lys Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys  
35 40 45  
20 Lys Met Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Gln Gly Gly Ile  
50 55 60  
Tyr Asp Phe Ile Gly Gln Phe Met Lys Ala Ser Val Asp Val Ala Asp  
65 70 75 80  
Leu Ile Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Gln  
85 90 95  
25 Tyr Lys Ile Met Val Ala Ala Leu Leu Gly Trp Ala Thr Ala Gln Leu Ile  
100 105 110  
Met Ser Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Gln Phe  
115 120 125  
30 Asp Trp Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val  
130 135 140  
His Tyr Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp  
145 150 155 160  
35 Leu Tyr His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser

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5 val Tyr Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu 165 170 175  
180 185 190  
Gly Ser Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu 195 200 205  
Ala Leu Ser Thr Leu Ala Leu Tyr Val Ala Val Val Asn Val His Ser 210 215 220  
225  
<210> 126  
<211> 258  
<212> PRT  
<213> Homo sapience

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<400> 126  
Met Ala Val Leu Ala Pro Leu Ile Ala Leu Val Tyr Ser Val Pro Arg 15  
1 5 10 15  
Leu Ser Arg Trp Leu Ala Gln Pro Tyr Tyr Leu Leu Ser Ala Leu Leu 20 25 30  
35  
Ser Ala Ala Phe Leu Leu Val Arg Lys Leu Pro Pro Leu Cys His Gly 40 45  
Leu Pro Thr Gln Arg Glu Asp Gly Asn Pro Cys Asp Phe Asp Trp Arg 50 55 60  
Glu Val Glu Ile Leu Met Phe Leu Ser Ala Ile Val Met Met Lys Asn 65 70 75 80  
Arg Arg Ser Met Phe Leu Met Thr Cys Lys Pro Pro Leu Tyr Met Gly 85 90 95  
Pro Glu Tyr Ile Lys Tyr Phe Asn Asp Lys Thr Ile Asp Glu Glu Leu 100 105 110  
Glu Arg Asp Lys Arg Val Thr Trp Ile Val Glu Phe Phe Ala Asn Trp 115 120 125  
Ser Asn Asp Cys Gln Ser Phe Ala Pro Ile Tyr Ala Asp Leu Ser Leu 130 135 140  
Lys Tyr Asn Cys Thr Gly Leu Asn Phe Gly Lys Val Asp Val Gly Arg 145 150 155 160  
Tyr Thr Asp Val Ser Thr Arg Tyr Lys Val Ser Thr Ser Pro Leu Thr 165

15

20 Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro Pro Phe Ile Ser Glu 15  
1 5 10 15  
Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp Tyr Cys Arg Thr Ser 20 25 30  
Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile Leu Gly Leu Thr Gly 35 40 45  
Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser Val Leu Leu Ser Leu 50 55 60  
Leu Leu Ile Leu Lys Ala Gly Arg Trp Asn Lys Tyr Phe Lys Ser 65 70 75 80  
Arg Arg Pro Leu Phe Thr Gly Leu Ile Gly Gly Leu Phe Thr Tyr 85 90 95  
Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val His Val Tyr 100 105 110  
<210> 128

25

30

35

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5 Lys Gln Leu Pro Thr Leu Ile Leu Phe Gln Gly Gly Lys Glu Ala Met 165 170 175  
180 185 190  
Arg Arg Pro Gln Ile Asp Lys Lys Gly Arg Ala Val Ser Trp Thr Phe 195 200 205  
Ser Glu Glu Asn Val Ile Arg Glu Phe Asn Leu Asn Glu Leu Tyr Gln 210 215 220  
Arg Ala Lys Lys Leu Ser Lys Ala Gly Asp Asn Ile Pro Glu Glu Gln 225 230 235 240  
Pro Val Ala Ser Thr Pro Thr Thr Val Ser Asp Gly Glu Asn Lys Lys 245 250 255  
Asp Lys

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<210> 127  
<211> 110  
<212> PRT  
<213> Homo sapience

15

<400> 127  
Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro Pro Phe Ile Ser Glu 15  
1 5 10 15  
Ala Ala Val Arg Gly Asn Ala Ala Val Leu Asp Tyr Cys Arg Thr Ser 20 25 30  
Val Ser Ala Leu Ser Gly Ala Thr Ala Gly Ile Leu Gly Leu Thr Gly 35 40 45  
Leu Tyr Gly Phe Ile Phe Tyr Leu Leu Ala Ser Val Leu Leu Ser Leu 50 55 60  
Leu Leu Ile Leu Lys Ala Gly Arg Trp Asn Lys Tyr Phe Lys Ser 65 70 75 80  
Arg Arg Pro Leu Phe Thr Gly Leu Ile Gly Gly Leu Phe Thr Tyr 85 90 95  
Val Leu Phe Trp Thr Phe Leu Tyr Gly Met Val His Val Tyr 100 105 110  
<210> 128

20

25

30

35

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<211> 91  
 <212> PRT  
 <213> Homo sapiens  
 5 <400> 128  
 Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser Gln Ser  
 1 5 10 15  
 Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile Ala Glu  
 20 25 30  
 Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Gln Asp Val Lys Lys  
 35 40 45  
 Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp Gly Arg  
 50 55 60  
 Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn His Leu  
 65 70 75 80  
 Arg Gly Pro Ser Pro Pro Met Ala Gly Gly  
 85 90  
 <210> 129  
 <211> 344  
 <212> PRT  
 <213> Homo sapiens  
 25 <400> 129  
 Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser  
 1 5 10 15  
 Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Leu Ala Leu  
 20 25 30  
 Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val  
 35 40 45  
 Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys  
 50 55 60  
 Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe  
 65 70 75 80  
 Arg Ile Phe Glu Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu  
 35

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85 90 95  
 Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Leu Ile Glu  
 100 105 110  
 Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser  
 115 120 125  
 Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser  
 130 135 140  
 Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr  
 145 150 155 160  
 Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly  
 165 170 175  
 Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys  
 180 185 190  
 Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser  
 195 200 205  
 Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser  
 210 215 220  
 Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp  
 225 230 235 240  
 Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe  
 245 250 255  
 Ser Gln Phe Ala Gln Gly Arg Arg Gln Arg Gln Gln Gly Gly Met  
 260 265 270  
 Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val  
 275 280 285  
 Asn Tyr Gln Gly Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu  
 290 295 300  
 Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg  
 305 310 315 320  
 Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val  
 325 330 335  
 Ala Thr Asn Phe Leu Leu Gln His  
 340  
 35 <210> 130

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&lt;211&gt; 428

&lt;212&gt; PRT

&lt;213&gt; Homo sapience

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Met Gly Pro Pro Gly Ala Gly Val Ser Cys Arg Gly Gly Cys Gly  
1 5 10 15Phe Ser Arg Leu Leu Ala Trp Cys Phe Leu Leu Ala Leu Ser Pro Gln  
20 25 3010 Ala Pro Gly Ser Arg Gly Ala Gly Ala Val Trp Thr Ala Tyr Leu Asn  
35 40 45Val Ser Trp Arg Val Pro His Thr Gly Val Asn Arg Thr Val Trp Gly  
50 55 60Leu Ser Glu Glu Gly Val Tyr Gly Gln Asp Ser Pro Leu Glu Pro Val  
65 70 75 8015 Ala Gly Val Leu Val Pro Pro Asp Gly Pro Gly Ala Leu Asn Ala Cys  
85 90 95Asn Pro His Thr Asn Phe Thr Val Pro Thr Val Trp Gly Ser Thr Val  
100 105 11020 Gln Val Ser Trp Leu Ala Leu Ile Gln Arg Gly Gly Cys Thr Phe  
115 120 125Ala Asp Lys Ile His Leu Ala Tyr Glu Arg Gly Ala Ser Gly Ala Val  
130 135 14025 Ile Phe Asn Phe Pro Gly Thr Arg Asn Glu Val Ile Pro Met Ser His  
145 150 155 160Pro Gly Ala Val Asp Ile Val Ala Ile Met Ile Gly Asn Leu Lys Gly  
165 170 175Thr Lys Ile Leu Gln Ser Ile Gln Arg Gly Ile Gln Val Thr Met Val  
180 185 19030 Ile Glu Val Gly Lys Lys His Gly Pro Trp Val Asn His Tyr Ser Ile  
195 200 205Phe Phe Val Ser Val Ser Phe Phe Ile Ile Thr Ala Ala Thr Val Gly  
210 215 22035 Tyr Phe Ile Phe Tyr Ser Ala Arg Arg Leu Arg Asn Ala Arg Ala Gln  
225 230 235 240

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Ser Arg Lys Gln Arg Gln Leu Lys Ala Asp Ala Lys Lys Ala Ile Gly  
245 250 255Arg Leu Gln Leu Arg Thr Leu Lys Gln Gly Asp Lys Glu Ile Gly Pro  
260 265 2705 Asp Gly Asp Ser Cys Ala Val Cys Ile Glu Leu Tyr Lys Pro Asn Asp  
275 280 285Leu Val Arg Ile Leu Thr Cys Asn-His Ile Phe His Lys Thr Cys Val  
290 295 30010 Asp Pro Trp Leu Leu Glu His Arg Thr Cys Pro Met Cys Lys Cys Asp  
305 310 315 320Ile Leu Lys Ala Leu Gly Ile Glu Val Asp Val Glu Asp Gly Ser Val  
325 330 335Ser Leu Gln Val Pro Val Ser Asn Glu Ile Ser Asn Ser Ala Ser Ser  
340 345 35015 His Glu Glu Asp Asn Arg Ser Glu Thr Ala Ser Ser Gly Tyr Ala Ser  
355 360 365Val Gln Gly Thr Asp Glu Pro Pro Leu Glu Glu His Val Gln Ser Thr  
370 375 38020 Asn Glu Ser Leu Gln Leu Val Asn His Glu Ala Asn Ser Val Ala Val  
385 390 395 400Asp Val Ile Pro His Val Asp Asn Pro Thr Phe Glu Asp Glu Thr  
405 410 415Pro Asn Gln Glu Thr Ala Val Arg Glu Ile Lys Ser  
420 425

25

&lt;210&gt; 131

&lt;211&gt; 1449

&lt;212&gt; DNA

&lt;213&gt; Homo sapience

30

&lt;400&gt; 131

atgaagcct tccaccttt ctgtgtgtc ctctgtgtt ttggagtggt ctctgaagcc

aagtttgatg attttgaggg tgaggaggac atagtagagt atgatgataa tgacttcgct

gaatttgagg atgtcatgga agactctgtt actgaatctc ctcaacgggt cataatcct

gaagatgatg aagatgagac cactgtggag ttggaggggc aggatgaaca ccaagaagga

35

60

120

180

240

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gattitgaag atgcagataac ccaaggagaga gatactgaga gtgaaccata tgaatgaga 300  
gaattgaaag gtatagaaaga caaacacagat acttcttcta gcaaaaataa agaaccaata 360  
acgattitg atgttcactgc aacotccag aacagctgg agatgatta tctagaatt 420  
ttgatgtgga ctgtctctg tgcctataac atgaattaca tcaattgggaa gaataaaac 480  
agtcgccttg ccaagacctg gtttaaacat cacaaggaga ttctggagag caactttact 540  
ttagtgaggag atgatggaa taaacaagaa gcaacaagaa caggaaaggt gaacaaggag 600  
aagagcaaa tctataaac gtgtgtct gtgcagagt gtctggagag catgtctac 660  
cagctgaagt tctctaaag acaagactta ctgaatgac tggcccgat gatgagaca 720  
gtgagtgaac aagtgaat aaaaatgaa atgaatgag aagaaatgaa taactactga 780  
ttgcgtctg gcaacaagaa agcctctgtg cgaataaga aagaaatgaa gatttgaat 840  
gaatttctga gtgataaac taagtctga gcaaatgat gactgcgga ctcttggac 900  
atcctgtcag agatgggaga agtcacagaa gaaatgatg atacaagat gtttaactt 960  
cttacaacct atgcagaaa gattgaact gtcaatttt cagacagat ctctgttca 1020  
aaaattatgc aagaaagaaag tcaactta aagtaactg acaataagag gaaactgtg 1080  
tttaacttta atgtgcctg ctcaaggaa acttaacca aagaaatgaa ggcactgta 1140  
ccctgatga acatgtgat ttacttact gataaagca aaaaattccg acttaacaga 1200  
gaaggaacac aaaaagcaga taagaacct gcccgatag aagaaactt ctgaaactg 1260  
aacatgtgc aagagcaaga agcagacag tctcgcgag aagaaagaaa aagagaaag 1320  
aagaaagcaa tcaatgaa gaaagatct gaagaaacag gaaagtctga ggaagtctga 1380  
ttggagctg agaaagaaag gttgaaag aagaaatga aaatgaaca aatcaaatg 1440  
aaagcaatg 1449

&lt;210&gt; 132

&lt;211&gt; 1002

25 &lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;400&gt; 132

atgtagaggt tggagacct gttatgccc tgggagcga ggtcagaaac acttctgtc 60  
ctacagtttg tcttctctt ctggaaatg ggcagatct gaactgggg ctctataagc 120  
ctctcttta caagatctg gctctcaat gtctgtatg cggcttggg gtatctggac 180  
cgaagaaagc caagcaggag gggccggac atccagaca taagtctg gactatagg 240  
aagtaaatga aagaaatct cccactctg ctgtcaaga ctgctgagct ggaacctct 300  
cgaataaca ttggagctt caacctcat ggaatctgg cgtcggagc ctcttgaaac 360  
ctgtgaaatg aagaaagag ctctctctg atcttcccg gataccgcc ccaatctgtg 420

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atgtctgaact tgtgtctcc gggccctctc ttcaagagat acaatcatg tgcagggtg 480  
gtcacatcag aaaaaggagag tgcgtctaac attctgaaac ggaagggttg cgaataactg 540  
ctggagcatca ttgtggggg tggccagag ggcctgatg ccaagcttg atcttcaacg 600  
ctgttaatgc ggaacccgaa gggctctgc aggtccgac tgaacacag ggaacacctg 660  
gtgcacatct tccctctcg ggaagatgac ctattgac agatcccaa ctctatgac 720  
tccgtgtac gctatcaaa gaaatctgt cagaagatca tgggcatctc cctcccaatc 780  
tttaatgac gtgtgtctct cagtaacag ttgttttaa taacctacg ccggccatc 840  
aacatctgag tgggagagac catcaggtta cagaagagac tgaatccctc ggaaggagag 900  
gtgaacacag tgaacagag ttatacaaa gaagtgtgaa acctcttga ggcacacaaa 960  
cttaagtta acaatccctgc tgaacagac ttgagattc gc 1002

&lt;210&gt; 133

&lt;211&gt; 801

&lt;212&gt; DNA

15 &lt;213&gt; Homo sapiens

&lt;400&gt; 133

atggagacct gggagctact caagacctgg gtctctgtgc ggaacgggca caactgtctg 60  
aacgtgggaa tcaagctgtc gctctctcg caagataacg agctggagca atgggagag 120  
caaggaggag tgcctctgc cctaaccttc ctgtactcag tgcgtggctc cctgtctctc 180  
taactcgtg tgcatacat ggaacctgac taagtgaat tgaagccca gctcaagag 240  
gaatcaaaag aagaaagaa agcaatgtt ccttcagaa tccctctcg gctctgaga 300  
taactgtcag tgcagagac cctgaagct cggacatgac gtgaatgccc cagtgtgctc 360  
cgaagctaac acaaacatg cctctgatg gaagaaatg tgggagagag caaacaccca 420  
ctcttctgag tcaactgag gctgaagctg gttgtgtctc ttgtgggct gtacttgga 480  
tgtcagagac tccgttctt ccaagacctg gttctgtgtg tgggtctcag cgggtctctg 540  
ttcgcaacct tccgtgtct gtccctcttc tggttgttg ccagactgct cctgtctcg 600  
caactctaac tgggtggcag caaacacac aactgggaat tcaatctctc acaacgcatc 660  
gcaatctcgc gccagagac cagcaaaccc ttcgaaacag gactgaaacg caactgtgac 720  
caactctctc gtgatagac ctcaaggtac tgggagacc tctgggtgga ggaaggagaa 780  
gaaggagaga gcccaatgtc t 801

&lt;210&gt; 134

&lt;211&gt; 318

&lt;212&gt; DNA

35

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&lt;21&gt; Homo sapiens

&lt;400&gt; 134

5 atgtccacta acatattgtc ggaaccnagg aggcggaaca aatgactgag gtacaaagccc 60  
ccgcagagcg aatgtacccc ggccttgagc gaaccgaagc cggactaat gaactgtgtg 120  
ggcatgatc taaagatgtg cggactaatg attaaagtga agtgggtgtc ttgggtcgt 180  
gtactatgt ccttaataag ctttgcaac tctggagct cggaggaac gaagaaatg 240  
atgtagtagt tcatgtgtc catctgtgc gtgggtgatg cctatctgca gaactctag 300  
cccatgagc cccatgg 318

10

&lt;210&gt; 135

&lt;211&gt; 672

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

15

&lt;400&gt; 135

atgacctgt ttaacttgg gaactgttc gctttgact acttcccta cttaacaa 60  
tacaagtga gggactgtc cgaatcaac gctttctgga aatgctca ggttgggtc 120  
acctacctt ttgtcaact ctgaagatg ctgttcttgg ccaatttctt tccncttgg 180  
gaaggcgca tctatgact catgtggag ttcataagg ccaagctgga tgtggagac 240  
ctgatagtc taaccttgt catgtcccg aatgcggca agggagagta caagatcatg 300  
gttctgccc tgggtgggc cactgtgag ctattatgt cccgtgat tccctatgg 360  
gtcggagccc ggggcatlga gtttactgg aatgacatc agatgagcat agactcaac 420  
atcagtttgg tccattacat cgtcgtctt gctcaggtct ggaatgatac acgtatgat 480  
ctgtacaaca ccttcggcc agctgtctc ctgtgatgt tctcagttgt ctacaaggcc 540  
tttattatgg agaccttct ccaactctgc tegtgggca gttggcagc tctactggcc 600  
cggcagttgg taacggggt gtgtggccc agcaatttgg cctgtatgt cgcgtgtgc 660  
aatgtgact cc 672

30

&lt;210&gt; 136

&lt;211&gt; 774

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

35

&lt;400&gt; 136

atgttttaca tctgaacgg acaagtgtg gacagccgga gtcagttccc atggagatta 60  
tcttgataa cagatttctt ctggggaata gctgagtttg tggttttgt ttcaaaact 120

atggcgtct tggcactct aattgtctc gtgtattcgg tgcgcgact ttcaagatgg 60  
ctgcacaa cttactact tctgtggcc ctgtctctg ctgccttct actcgtagg 120  
aaactgcgc cgtctgtcca cgtctgccc acccaacggc aagacggtaa cccgtgtgac 180  
tttactgga gagaagtga gactgtgtg tttctcagtg ccatgtgat gatgaagac 240  
cgcagatcca tgttctgat gacgtgaaa ccccactat atatggccc tgaatatac 300  
aagtactca atgataaac cattgatg gaactagac gggcaagag ggtcaacttgg 360  
atggcaggt tcttgcca ttgtctaat gactgcaat cattgcccc tatctatgt 420  
gaactctcc ttaatacaa ctgtacagg ctcaatttg ggaagtgga tgttggagc 480  
tatactgat ttactcgg gtacaaagt agcacatcac cctcaacaa gaactcctt 540  
acctgatcc tgttccagg tggcaaggc gaatgggc ggcacagat tgaagaaga 600  
ggcaggctg tctcatgac ctctctgag gagaatgta tccgagaatt taacttaatt 660  
gagctatac agcgggcaa gaactatca aaggttggg acaatatccc tgaagagag 720  
cctgtgctt caacccccc cacagtgtc gatgggaaa acaagaaggg taaa 774

15

&lt;210&gt; 137

&lt;211&gt; 330

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

20

&lt;400&gt; 137

atggcgcgg tgttggcaa ggggaaggc ccgcgttca tcaagagggc ggcgttggc 60  
ggcaacggc cgtcttggg ttatggcg acctcgtgt cagcgtgtc gggggcagc 120  
ggcggcatc tggcctcac cggcctcac ggttctatct tctactgt cgcctcgtc 180  
ctgtctccc tgcctcat tctcaaggc ggaaggagt ggaacaaata ttcaaatca 240  
cggagacctc tctttacag agcctcac gggggctct tcaactact cctgttttg 300  
accttctct acggcatggt gacgtctac 330

&lt;210&gt; 138

&lt;211&gt; 273

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

30

&lt;400&gt; 138

atgttttaca tctgaacgg acaagtgtg gacagccgga gtcagttccc atggagatta 60  
tcttgataa cagatttctt ctggggaata gctgagtttg tggttttgt ttcaaaact 120

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ctgctcagc aagatctgaa aaaaagaa agatctgaa acatcatcga ttccagatat 180  
gatgatggaa yaggggcacac agaaacccct ccccgagaa tgggtagaat caatcatctg 240  
ctgagcccta gtcacccctc aatgctcgtt gga 273

5

<210> 139  
<211> 1032  
<212> DNA  
<213> Homo sapience

10

<400> 139  
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ttctgtatg accttcacag agtaaaagaa gaattccaga ttctggaggt gatatgtgaa 180  
agataattt ggcctgattt gaagatact ttctcgagta gtcgctctat ttataatttt 240  
aggataattt aagaagata tggaaagcaga aaatttgcct ccttttgcct ggtctccctg 300  
gtttttcag ccttatttga cttccctcct attgaaagta tgaagtaatt ctttgacatc 360  
acrgacgcta gtaatttgcg ttctcgatcc ctggacactg tgtttgctct gttctgacaa 420  
ttttactcgt ccatccacag agtccaaatg gcaaaattc tgggtccgct gtccatccaa 480  
aaacaaagat tgatttatat atttggactg cagctttcca cctctgctc ctacatctgg 540  
aatgtgacaa taagtggact taatgcctgt ctgtgcacg aacgaaatat gttccaaatg 600  
catcaagtgc tctgcatccg aagcttgatg gcaaaattct ttctctggac acttgaacc 660  
atcttctct cttcagaacg caccagcgaa gccaaattt ggaatggagc caagctggac 720  
atccaaagac agcagaagat ggaatgctg gacggcgac tgaatctc tcaatttga 780  
caagggaggg gacagagaa gcaagagga gaaatgata attgaaatg tcttttct 840  
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ctgctgcagc ac 1032

15

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aggataattt aagaagata tggaaagcaga aaatttgcct ccttttgcct ggtctccctg 300  
gtttttcag ccttatttga cttccctcct attgaaagta tgaagtaatt ctttgacatc 360  
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ctgctgcagc ac 1032

20

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caagggaggg gacagagaa gcaagagga gaaatgata attgaaatg tcttttct 840  
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cccctctag aagttctga ggaacaggtc gcccgctca tggagatgg atttccaga 960  
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ctgctgcagc ac 1032

25

<210> 140  
<211> 1284  
<212> DNA  
<213> Homo sapience

30

&lt;400&gt; 140

156/177

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ctgcatctgt gttcctctgt ggccttgat ccgaaagcac ccggttccg gggggctgaa 120  
gaaatctgaa ccggctacct caagctgac tggcggttc ccgaaaggg atgaacgtt 180  
acggctggg agctgagaga ggaagcggtg taaggcagag actcgacct ggaatctgtg 240  
gctgggtctc tggtaagcc cgaagggccg gggcgctta acgctgtaa ccgcaaacg 300  
aatccacg tgcacacgtt ttgggaagc acggtgaa tctcttggt ggcctctac 360  
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ccgggtgag tagaatgt tgaatcatg atcggaatc tgaagagac aaaaattctg 540  
caactcttc aagaagagat aaagtacaa atgtctag aagtaggaa aaaaatggc 600  
ccttgggtga atcaatc attttttc gttctggt ccttttat tatcagcg 660  
gcaatctggt gctatttat ctttatct gctcgaaagc taaggatgc aagaatcaa 720  
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cctgtacca atgaatc taatgtgc tctccatg aagaatgaa tccgagag 1080  
aagcatcat ctgtatgc ttcaatagc ggaacagatg aacgcctct ggaagacac 1140  
gtgaaatcaa caaatgaaag tctaaagct gtaaacatg aagaatc tgttgacgt 1200  
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actgcgttc gagaatcaa atct 1284

25

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<213> Homo sapience

30

<221> CDS  
<222> (122)...(1573)

&lt;400&gt; 141

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tcgaaagag ggcgtggc cgggttcgg ctggcgac agcttttt ctcaaggtgc 120  
a atg aaa gcc ttc cac act ttc tgt gtc gtc ctt ctg gtc ttt ggg 166

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Met Lys Ala Phe His Thr Phe Cys Val Val Leu Leu Val Phe Gly

1 10 5 15

agt gtc tct gaa gcc aag ttt gat gat ttt gag gat gag gag aac ata

Ser Val Ser Glu Ala Lys Phe Asp Asp Phe Glu Asp Glu Glu Asp Ile

20 25 30

gta gag tat gat gat aat gac ttc gct gaa ttt gag gat gtc atg gaa

Val Glu Tyr Asp Asp Asn Asp Phe Ala Glu Phe Glu Asp Val Met Glu

35 40 45

gac tct gtt act gaa tct cct caa cgg gtc ata atc act gaa gat gat

Asp Ser Val Thr Glu Ser Pro Gln Arg Val Ile Thr Glu Asp Asp

50 55 60

gaa gat gag acc act gtc gag ttg gaa ggg cag gat gaa aac caa gaa

Glu Asp Glu Thr Thr Val Glu Leu Glu Gly Gln Asp Glu Asn Gln Glu

65 70 75

gga gat ttt gaa gat gca gat acc cag gag gga gat act gag agt gaa

Gly Asp Phe Glu Asp Ala Asp Thr Gln Glu Gly Asp Thr Glu Ser Glu

80 85 90 95

cca tat gat gat gaa gaa ttt gaa ggt tat gaa gac aac cca gat act

Pro Tyr Asp Asp Glu Glu Phe Glu Gly Tyr Glu Asp Lys Pro Asp Thr

100 105 110

tct tct agc aac aat aaa gac cca ata acg att gtt gat gtt cct gca

Ser Ser Ser Lys Asn Lys Asp Pro Ile Thr Ile Val Asp Val Pro Ala

115 120 125

cac ctc cag aac agc tgg gag agt tat tat cta gaa att ttg atg gtc

His Leu Gln Asn Ser Trp Glu Ser Tyr Tyr Leu Glu Ile Leu Met Val

130 135 140

act ggt etg ctt gct tat atc atg aat tac atc att ggg aag aat aaa

Thr Gly Leu Leu Ala Tyr Ile Met Asn Tyr Ile Ile Gly Lys Asn Lys

145 150 155

aac agt cgc ctt gca cag gcc tgg ttt aac act cat agg gag ctt ttg

Asn Ser Arg Leu Ala Gln Ala Trp Phe Asn Thr His Arg Glu Leu Leu

160 165 170 175

gag agc aac ttt act tta gtc ggg gat gat gga act aac aac gaa gcc

Glu Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala

180 185 190

gag agc aac ttt act tta gtc ggg gat gat gga act aac aac gaa gcc

Glu Ser Asn Phe Thr Leu Val Gly Asp Asp Gly Thr Asn Lys Glu Ala

190 195 200

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aca agc aca gga aag ttg aac cag gag aat gag cac atc tat aac ctg

Thr Ser Thr Gly Lys Leu Asn Gln Glu Asn Glu His Ile Tyr Asn Leu

195 200 205

tgg tgt tct ggt cga gtc tgc gag ggc atg att atc cag ctg agg

5 Trp Cys Ser Gly Arg Val Cys Cys Glu Gly Met Leu Ile Gln Leu Arg

210 215 220

ttc ctc aag aga caa gac tta ctg aat gtc ctg gcc cgg atg atg agg

Phe Leu Lys Arg Gln Asp Leu Leu Asn Val Leu Ala Arg Met Met Arg

225 230 235

cca gtc agt gat caa gtc caa ata aaa gta acc atg aat gat gaa gac

Pro Val Ser Asp Gln Val Ile Lys Val Thr Met Asn Asp Glu Asp

240 245 250 255

atg gat acc tac gta ttt gct gtt ggc aca cgg aaa gcc ttg gtc cga

Met Asp Thr Tyr Val Phe Ala Val Gly Thr Arg Lys Ala Leu Val Arg

260 265 270

cta cag aaa gag atg cag gat ttg agt gag ttt tgt agt gat aac cct

Leu Gln Lys Glu Met Gln Asp Leu Ser Glu Phe Cys Ser Asp Lys Pro

275 280 285

aag tct gga gca aag tat gga ctg cgg gac tct ttg gcc atc ctg tea

Lys Ser Gly Ala Lys Tyr Gly Leu Pro Asp Ser Leu Ala Ile Leu Ser

290 295 300

gag atg gga gaa gtc aca gac gga atg atg gat aca aag atg gtt cac

Glu Met Gly Glu Val Thr Asp Gly Met Met Asp Thr Lys Met Val His

305 310 315

ttt ctt aca cac tat gct gac aag att gaa tct gtt cat ttt tca gac

Phe Leu Thr His Tyr Ala Asp Lys Ile Glu Ser Val His Phe Ser Asp

320 325 330 335

cag ttc tct ggt cca aaa att atg caa gag gaa ggt cag cct tta aag

Gln Phe Ser Gly Pro Lys Ile Met Gln Glu Glu Gly Gln Pro Leu Lys

340 345 350

cta cct gac act aag agg aca ctg ttg ttt aca ttt aat gtc cct ggc

Leu Pro Asp Thr Lys Arg Thr Leu Leu Phe Thr Phe Asn Val Pro Gly

355 360 365

tca ggt aac act tac cca aag gat atg gag gca ctg cta ccc ctg atg

Ser Gly Asn Thr Tyr Pro Lys Asp Met Glu Ala Leu Leu Pro Leu Met

365 370 375



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370 375 380  
 aac atg gtc att tat tct att gat aaa ggc aaa aag ttc cga cta aac 1318  
 aac met val ile tyr ser ile asp lys ala lys phe arg leu aac 385  
 390 395  
 5 aga gaa ggc aac caa aaa gca gat aag aac cgt gcc cga gta gaa gag 1366  
 arg glu gly lys gln lys ala asp lys aac arg ala arg val glu glu 400  
 405 410 415  
 aac ttc ttg aaa ctg aca cat gtc caa aga cag gaa gca gca cag tct 1414  
 aac phe leu lys leu thr his val gln arg gln ala ala gln ser  
 10 420 425 430 435  
 cgg cgg gag gag aaa aaa aga gaa gag aag gag cga atc atg aat gag 1462  
 arg arg glu glu lys lys arg ala glu lys glu arg ile met aac glu 435  
 440 445  
 gaa gat cct gag aaa cag cgc agg ctg gag gag gct gca ttg agg cgt 1510  
 glu asp pro glu lys gln arg arg leu glu glu ala leu arg arg 450  
 455 460  
 gag caa aag aag ttg gaa aag aag caa atg aaa atg aaa atc aac 1558  
 glu gln lys lys leu glu lys gln met lys met lys gln ile lys 465  
 470 475  
 20 gtc aaa gcc atg taagcacc cccagagatt gattctgat gccacctgta 1610  
 val lys ala met 480  
 agctcgaat taacagaaa catgaaaaa gccagccaat ttctcaacct taatttcag 1670  
 acaagcttgg gccacctgaga aatccttatt taataaccta ctctgtttgg gggtttgggt 1730  
 tttaacagaga ttgaagatcc ctggaaaggg ctctgtttca agaatcttt ttccaagata 1790  
 atcaaatatt ttgtattatt ttataaagg aatgatttat gaatatctg taggttttaa 1850  
 atattttaa aattatata caaatcatca gtgcttttg taactcaagt tttaagaaa 1910  
 taacatgaaa ttatagytta gataaccaga ttgttgcttt ttgtttaac caagagctg 1970  
 aaatgctat aagaactgac tctaaccaa gattctgcaa ataagattg gaattgaca 2030  
 ataacattg ctgattgctt 2050  
 30  
 <210> 142  
 <211> 2746  
 <212> DNA  
 <213> Homo sapiens

160/177

<220>  
 <221> CDS  
 <222> (70)...(1074)  
 5 <400> 142  
 aaacactgtg ggtgactcag aacacagag agctcacaga accctgggga gccagctga 60  
 cccgcagc atg gta gag ttc gcg ccc ttg ttt atg ccg tgg gag cgc 108  
 met val glu phe ala pro leu phe met pro trp glu arg  
 1 5 10  
 10 agg ctg cag aca ctt gct gtc cta cag ttc gtc ttc tcc ttg gca 156  
 arg leu gln thr leu ala val leu gln phe val phe ser phe leu ala 20  
 25  
 ctg gcc gag atc tgc act gtc ggc ttc ata gcc ctg ctg ttc aca aga 204  
 leu ala glu ile cys thr val gly phe ile ala leu leu phe thr arg 30  
 35 40 45  
 ttc tgg ctg ctg act gtc ctg tat gcg gcc tgg tgg tat ctg gaa cga 252  
 phe trp leu leu thr val leu tyr ala ala trp tyr leu asp arg 50  
 55 60  
 20 gac aag caa cgg aag ggg ggc cgc cac atc cag gcc atc agg tgc tgg 300  
 asp lys pro arg gln gly arg his ile gln ala ile arg cys trp 65  
 70 75  
 act ata tgg aag tac atg aag gac tat ttc ccc atc tgg ctg gtc aag 348  
 thr ile trp lys tyr met lys asp tyr phe pro ile ser leu val lys 80  
 85 90  
 25 act gct gag ctg gac ccc tct cgg aac tac atc gcg ggc ttc cac ccc 396  
 thr ala glu leu asp pro ser arg aac tyr ile ala gly phe his pro 95  
 100 105  
 cat gga gtc ctg gaa gtc gga gcc ttc gcc aac ctg tgc act gag agc 444  
 his gly val leu ala val gly ala phe ala aac leu cys thr glu ser 110  
 115 120 125  
 aca ggc ttc tct tgg atc ttc ccc ggt atc cgc ccc cat ctg atg atg 492  
 thr gly phe ser ile phe pro gly ile arg pro his leu met met 130  
 135 140  
 ctg acc ttg tgg ttc cgg gcc ccc ttc ttc aga gat tac atc atg tct 540  
 leu thr leu trp phe arg ala pro phe phe arg asp tyr ile met ser 145



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<221> CDS  
<222> (32)...(835)  
<400> 143  
attcttcagg gtcggggccc gggccgagagc g atc ggc ccc tgg ggc ctc ctc  
Met Ala Pro Trp Ala Leu Leu  
1 5  
5  
ago ccc ggg gtc ctc gtc cgg aac ggg ccc acc gtc ctc acc tgg gga  
Ser Pro Gly Val Leu Val Arg Thr Gly His Thr Val Leu Thr Trp Gly  
10 15 20  
acc aag ctc gtc ctc ttc ctc ccc gat acc gag ctc cgg caa tgg gag  
Ile Thr Leu Val Leu Phe Leu His Asp Thr Glu Leu Arg Glu Trp Glu  
25 30 35  
gag cag ggg gag ctc ctc ctc ccc ctc acc ttc ctc ctc ctc gtc ctc  
Glu Glu Gly Glu Leu Leu Leu Pro Leu Thr Phe Leu Leu Val Leu  
40 45 50 55  
ggc tcc ctc ctc tcc tcc ctc gct gtc tca ctc atg gag ccc ggc tac  
Gly Ser Leu Leu Leu Tyr Leu Ala Val Ser Leu Met Asp Pro Gly Tyr  
60 65 70  
gtg aac gtc cag ccc cag ccc cag gag gag ctc aaa gag gag cca  
Val Asn Val Glu Pro Glu Pro Glu Glu Leu Lys Glu Glu Thr  
75 80 85  
ggc atg gtc ccc cca gcc atc ccc ctc cgg cgc tgc aga tac tgc ctc  
Ala Met Val Pro Pro Ala Ile Pro Leu Arg Arg Cys Arg Tyr Cys Leu  
90 95 100  
gtg ctc cag ccc ctc agg gct cgg ccc tgc cgt gag tgc cgc cgt tgc  
Val Leu Glu Pro Leu Leu Arg Ala Arg His Cys Arg Glu Cys Arg Cys  
105 110 115  
ggc cgc cgc tac gag ccc ccc tgc ccc tgg atg gag aac tgc gtc gga  
Val Arg Arg Tyr Asp His His Cys Pro Trp Met Glu Asn Cys Val Gly  
120 125 130 135  
gag cgc aac ccc cca ctc ttt gtc gtc tac ctc gag ctc cag ctc gtc  
Glu Arg Asn His Pro Leu Phe Val Val Tyr Leu Ala Leu Leu Val  
140 145 150  
gtg ctc ctc tgg ggc ctc tac ctc gca tgg tca gcc ctc cgc ttc ctc  
35 532

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Val Leu Leu Trp Gly Leu Tyr Leu Ala Trp Ser Gly Leu Arg Phe Phe  
155 160 165  
cag ccc tgg gtc ctc tgg ttc cgg tcc agc ggg ctc ctc ttc gcc acc  
Glu Pro Trp Gly Leu Trp Leu Arg Ser Ser Gly Leu Leu Phe Ala Thr  
170 175 180  
ttc ctc ctc ctc tcc ctc ttc tcc ttc gtc ggc agc ctc ctc ctc gtc  
Phe Leu Leu Leu Ser Leu Phe Ser Leu Val Ala Ser Leu Leu Val  
185 190 195  
tcg ccc ctc tac ctc gtc gtc gcc agc aac acc acc acc tgg gaa ttc atc  
Ser His Leu Tyr Leu Val Ala Ser Asn Thr Thr Trp Glu Phe Ile  
200 205 210 215  
tcc tca ccc cgc atc gcc tat ctc cgc cag cgc ccc agc aac ccc ttc  
Ser Ser His Arg Ile Ala Tyr Leu Leu Arg Glu Arg Pro Ser Asn Pro Phe  
220 225 230  
gac cga ggc ctc acc cgc aac ctc gcc ccc ccc ttc ttc tgc gga tgg ccc  
Asp Arg Gly Leu Thr Arg Asn Leu Ala His Phe Cys Gly Trp Pro  
235 240 245  
tca ggg tcc tgg gag acc ctc tgg gct gag gag gag gaa gag ggc agc  
Ser Gly Ser Trp Glu Thr Leu Trp Ala Glu Glu Glu Gly Ser  
250 255 260  
agc cca gct gtc taggttgcg ggaagccggg ctaccgcttc gtgcctga  
Ser Pro Ala Val  
265  
aaaccacagg gacgtccccc agctgggtg agcgtcaga gggcctgggg ccctcactcc  
tgcaccagcc tcccgagccc cagaacggag ctccaagcca gacagatccc tgccttggtg  
ggcagttcgg ccttcocagg aagaaggga agaaaggac ctgtgggtgg ctcaaggcca  
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attaatata aagcagctcc agcttc  
930 990 1050 1110 1136  
30  
<210> 144  
<211> 619  
<212> DNA  
<213> Homo sapiens  
<220>  
<221> CDS  
35

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166/177

&lt;222&gt; (13)...(333)

&lt;221&gt; CDS

&lt;222&gt; (111)...(785)

&lt;400&gt; 144

cttgcactcg ct atg tcc act aac aat atg tcy gac cca cgg agg ccg 48

Met Ser Thr Asn Asn Met Ser Asp Pro Arg Arg Pro

1

5

10

aac aea gty ctg agg tac aag ccc ccg ccg agc gaa tgt aac ccg gcc 96

Asn Lys Val Leu Arg Tyr Lys Pro Pro Pro Ser Glu Cys Asn Pro Ala

15

20

25

ttg gac gac ccg ccg gac tac atg aac ctg ctg ggc atg atc ttc 144

Leu Asp Asp Pro Thr Pro Asp Tyr Met Asn Leu Leu Gly Met Ile Phe

30

35

40

agc atg tgc ggc ctc atg ctt aag ctg aag tgg tgt gct tgg gtc gct 192

Ser Met Cys Gly Leu Met Leu Lys Leu Lys Trp Cys Ala Trp Val Ala

45

50

55

gtc tac tgc tcc ttc atc agc ttt gcc aac tct cgg agc tcy gag gac 240

Val Tyr Cys Ser Phe Ile Ser Phe Ala Asn Ser Arg Ser Ser Glu Asp

60

65

70

acg aag caa atg atg agt agc ttc atg ctg tcc atc tct gcc gtg gtg 288

Thr Lys Gln Met Met Ser Phe Met Leu Ser Ile Ser Ala Val Val

80

85

90

atg tcc tat ctg cag aat cct cag ccc atg acg ccc cca tgg 340

Met Ser Tyr Leu Gln Asn Pro Gln Pro Met Thr Pro Pro Trp

95

100

105

tgataccagc ctagaagggt cacatttgg accctgtcta tccactaggc ctgggcttg 390

gtcgtataac ctgctgctt cagctgccat cctggacttc cctgaatag ggcgtctcg 450

tgccccccagc tggatagagg gaacctggcc ctcttctagg gaacacctta ggcctaccce 510

tctgcctcc ctctccctgc ctgctgctgg gggagatgct gtccatgttt ctagggtat 570

tcatttgctt tctagttaga acctgttgtt aataaagttt ttcactcag 619

30

&lt;210&gt; 145

&lt;211&gt; 864

&lt;212&gt; DNA

&lt;213&gt; Homo sapiens

&lt;220&gt;

5

&lt;400&gt; 145

agggtgggtgc caggccctgg ccgtggcgaa agagccgggg gagccggaga ccagctcccg 60

ggagccgc ctcgcgctacc ccgcgcgggc gggaccgggc ggcgcgcatc atg acc 116

Met Thr

1

164

ctg ttt cac ttc ggg aac tgc ttc gct ctt gcc tac ttc ccc tac ttc

Leu Phe His Phe Gly Asn Cys Phe Ala Leu Ala Tyr Phe Pro Tyr Phe

5

10

15

212

atc acc tac aag tgc agc ggc ctg tcc gag tac aac gcc ttc tgg aac

Ile Thr Tyr Lys Cys Ser Gly Leu Ser Glu Tyr Asn Ala Phe Trp Lys

20

25

30

260

tgc gtc cag gct gga gtc acc tac ctc ttt gtc caa ctc tgc aag atg

Cys Val Gln Ala Gly Val Thr Tyr Leu Phe Val Gln Leu Cys Lys Met

35

40

45

50

308

ctg ttc ttg gcc act ttc ttt ccc acc tgg gaa ggc ggc atc tat gac

Leu Phe Leu Ala Thr Phe Phe Pro Thr Trp Glu Gly Ile Tyr Asp

55

60

65

356

ttc att ggg gag ttc atg aag gcc agc gtg gat gtg gca gac ctg ata

Phe Ile Gly Glu Phe Met Lys Ala Ser Val Asp Val Ala Asp Leu Ile

70

75

80

404

ggc cta aac ctt gtc atg tcc cgg aat gcc ggc aag gga gag tac aag

Gly Leu Asn Leu Val Met Ser Arg Asn Ala Gly Lys Gly Glu Tyr Lys

85

90

95

452

atc atg gtt gct gcc ctg ggc tgg gcc act gct gag ctt att atg tcc

Ile Met Val Ala Ala Leu Gly Trp Ala Thr Ala Glu Leu Ile Met Ser

100

105

110

500

cgc tgc att ccc cta tgg gtc gga gcc cgg ggc att gag ttt gac tgg

Arg Cys Ile Pro Leu Trp Val Gly Ala Arg Gly Ile Glu Phe Asp Trp

115

120

125

130

548

aag tac atc cag atg agc ata gac tcc aac atc agt ctg gtc cat tac

Lys Tyr Ile Gln Met Ser Ile Asp Ser Asn Ile Ser Leu Val His Tyr

135

140

145

35

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atc gtc ggc tct gct cag gtc tgg atg ata aca cgc tat gat ctg tac 596  
Ile Val Ala Ser Ala Gln Val Trp Met Ile Thr Arg Tyr Asp Leu Tyr  
150 155 160  
cac acc ttc cgg cca gct gtc ctc ctg atg ttc ctc agt gtc tac 644  
His Thr Phe Arg Pro Ala Val Leu Leu Leu Met Phe Leu Ser Val Tyr  
165 170 175  
aag gcc ttt gtt atg gag acc ttc gtc cac ctc tgc tgg ctg ggc agt 692  
Lys Ala Phe Val Met Glu Thr Phe Val His Leu Cys Ser Leu Gly Ser  
180 185 190  
tgg gca gct cta ctg ggc cga gaa gtc gta aag ggg ctg ctg ggc ctc 740  
Trp Ala Ala Leu Leu Ala Arg Ala Val Val Thr Gly Leu Leu Ala Leu  
195 200 205 210  
agc act ttg ggc ctg tat gtc ggc gtc gtc gtc cag tcc tagcttgg 790  
Ser Thr Leu Ala Leu Tyr Val Ala Val Asn Val His Ser  
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1 5  
ctc gtc tat tgg gtc cgg cga cct tca cga tgg ctg ggc caa cct tac 99  
Leu Val Tyr Ser Val Pro Arg Leu Ser Arg Trp Leu Ala Gln Pro Tyr  
10 15 20 25  
taa ctc ctg tgg ggc ctg ctc tct gct ggc ttc cta ctc gtc agg aaa 147  
Tyr Leu Leu Ser Ala Leu Leu Ser Ala Ala Phe Leu Leu Val Arg Lys

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ctg cgg cgg ctc tgc caa ggt ctg ccc acc caa cgc gaa ggc agc 195  
Leu Pro Pro Leu Cys His Gly Leu Pro Thr Gln Arg Glu Asp Gly Asn  
45 50 55  
cgg tgc gac ttt gac tgg age gaa gtc gag atc ctg atg ttc ctc agt 243  
Pro Cys Asp Phe Asp Trp Arg Glu Val Glu Ile Leu Met Phe Leu Ser  
60 65 70  
gac att gtc atg atg aag aac cgc aga tcc atg ttc ctg atg aag tgc 291  
Ala Ile Val Met Met Lys Asn Arg Arg Ser Met Phe Leu Met Thr Cys  
75 80 85  
aaa ccc ccc cta tat atg ggc cct gag tat atc aag tac ttc aat gat 339  
Lys Pro Pro Leu Tyr Met Gly Pro Glu Tyr Ile Lys Tyr Phe Asn Asp  
90 95 100 105  
aaa acc att gat gag gaa cta gaa cgg gag aag agg gtc act tgg att 387  
Lys Thr Ile Asp Glu Leu Leu Glu Arg Asp Lys Arg Val Thr Trp Ile  
110 115 120  
gtg gag ttc ttt gac aat tgg tct aat gac tgc caa tca ttt ggc cct 435  
Val Glu Phe Phe Ala Asn Trp Ser Asn Asp Cys Gln Ser Phe Ala Pro  
125 130 135  
atc tat gct gac ctc tcc cct aaa tac aac tgt aca ggg cta aat ttt 483  
Ile Tyr Ala Asp Leu Ser Leu Lys Tyr Asn Cys Thr Gly Leu Asn Phe  
140 145 150  
ggg aag gtc gat gtc gga cgc tat act gat gtc agt aag cgg tac aaa 531  
Gly Lys Val Asp Val Gly Arg Tyr Thr Asp Val Ser Thr Arg Tyr Lys  
155 160 165  
gtg ago aca tca ccc ctc acc aag caa ctc cct acc ctg atc ctg ttc 579  
Val Ser Thr Ser Pro Leu Thr Lys Gln Leu Leu Pro Thr Leu Ile Leu Phe  
170 175 180 185  
caa ggt ggc aag gag gca atg cgg cgg cca cag att gac aag aaa gga 627  
Gln Gly Gly Lys Glu Ala Met Arg Arg Pro Gln Ile Asp Lys Lys Gly  
190 195 200  
cgg gct gtc tca tgg acc ttc tct gag gag aat gtc atc cga gaa ttt 675  
Arg Ala Val Ser Trp Thr Phe Ser Glu Glu Asn Val Ile Arg Glu Phe  
205 210 215  
aac tta aat gag cta tac cag cgg ggc aag aaa cta tca aag gct gga 723

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5	Asn Leu Asn Glu Leu Tyr Gln Arg Ala Lys Lys Leu Ser Lys Ala Gly	220	225	230	771
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	Asp Asn Ile Pro Glu Glu Gln Pro Val Ala Ser Thr Pro Thr Thr Val	235	240	245	
	tca gat ggg gaa aac aag aag gat aaa taagatcctc ac				810
	Ser Asp Gly Glu Asn Lys Lys Asp Lys	250	255		
10	tttggcngtg cttcctctcc tgcataatcc aggtctcttc cataaccaca agcctgagge	870			
	tgcagcttt tatttatgtt ttccctttgg ctgtgaetgg gtggggcage atgcagcttc	930			
	tgattttaaa gaggeateta ggggaattgc aggaacctca caggagggcc tgcctatgctg	990			
	tgcccaactg ttteactgga gcaagaaaga gatctcatag gaaggagggg gaaatggttt	1050			
	ccctccagc ttgggtcagt gtgttaactg cttatcagct attcagcact ctcctatggtt	1110			
	ttcccatgaa actctgtggt ttcatccttc cttcttagtt gaactgcaca gcttggttag	1170			
15	acctagatt aacctaaagg taagatgctg gggatagaa cgttaagaat ttcccccac	1230			
	ggactcttgc ttccctttagc cctcttggt tegttaaggg tcttcattaa agtataagc	1290			
	ctaactttgt cgtctagctc aaggagaac ctttaaccac aaagttttta tcaatgaaga	1350			
	caatattgaa caaccacctca ttttggggg attgagaagg ggtgaataga gctttgagac	1410			
	tttctttgt gtggtaggac ttgagggaga aatcccttgg acttcaacta accctctgac	1470			
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	gcgccgggc tgggtgcg atg gcc gcg gtg gtg gcc aag cgg gaa ggg ccg	170			
	Met Ala Ala Val Val Ala Lys Arg Glu Gly Pro				
	1 5 10				
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Met Val Tyr Ile Ser Asn Gly Gln Val Leu Asp Ser Arg Ser  
1 5 10  
cag tct cca tgg aga tta tct ttg ata aca gat ttc ttc tgg gga ata 157  
Gln Ser Pro Trp Arg Leu Ser Leu Ile Thr Asp Phe Phe Trp Gly Ile  
15 20 25 30  
gct gag ttt gtc gtc ttt ttc aac aac ctg ctt cag caa gat gtc 205  
Ala Gln Phe Val Val Leu Phe Phe Lys Thr Leu Leu Gln Asp Val  
35 40 45  
aaa aaa aga aga agc tat gga aac tca tct gat tcc aga tat gat 253  
Lys Lys Arg Arg Ser Tyr Gly Asn Ser Ser Asp Ser Arg Tyr Asp Asp  
50 55 60  
gga aga ggg cca cca gga aac cct ccc cga aga atg ggt aga atc aat 301  
Gly Arg Gly Pro Pro Gly Asn Pro Pro Arg Arg Met Gly Arg Ile Asn  
65 70 75  
cat ctg cgt ggc cct agt ccc cct cca atg gct ggt gga tggagaggt 350  
His Leu Arg Gly Pro Ser Pro Pro Met Ala Gly Gly  
80 85 90  
aaatgctcgc tctaaagac agacaacgg ncatgagat tcatagaga agyaaacat 410  
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tgctctgtgt cctcaagat gaatgagtc atgctggaa ttcctctgc agygaactg 530  
cctgactgaa atgagctcc ataatgag atgttggct catcaactc tggatagct 590  
tattaagta ttaatatgt ttaataagt aaatatctt aggttgaga atgactcct 650  
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Met Phe Thr Ser Thr Gly Ser Ser Gly Leu Tyr Lys Ala Pro Leu Ser  
1 5 10 15  
aag agc ctt ctg ctg gtc ccc agt gcc ctc tcc ctc ctg ctc gcc ctc 151  
Lys Ser Leu Leu Leu Val Pro Ser Ala Leu Ser Leu Leu Ala Leu  
20 25 30  
ctc ctg cct ccc tgc cag aag ctc ttc gtc tac gac ctt cag gca gtc 199  
Leu Leu Pro His Cys Gln Lys Leu Phe Val Tyr Asp Leu His Ala Val  
35 40 45  
aag aac gac ttc cag att tgg agg ttg ata tgf gga aga ata atc tgc 247  
Lys Asn Asp Phe Gln Ile Trp Arg Leu Ile Cys Gly Arg Ile Ile Cys  
50 55 60  
ctt gat ttg aaa gat acc ttc tgc agt agt ctg ctt att tat aat ttt 295  
Leu Asp Leu Lys Asp Thr Phe Cys Ser Ser Leu Leu Ile Tyr Asn Phe  
65 70 75 80  
agg ata ttt gaa aga aga tat gga agc aga aaa ttt gca too ttt ttg 343  
Arg Ile Phe Gln Arg Arg Tyr Gly Ser Arg Lys Phe Ala Ser Phe Leu  
85 90 95  
ctg ggt tcc tgg gtc ttg tca gcc tta ttt gac ttt ctc ctc att gaa 391  
Leu Gly Ser Trp Val Leu Ser Ala Leu Phe Asp Phe Leu Ile Gln  
100 105 110  
gct atg cag tat ttc ttt ggc atc acc gca gct agt aat ttg cct tct 439  
Ala Met Gln Tyr Phe Phe Gly Ile Thr Ala Ala Ser Asn Leu Pro Ser  
115 120 125  
gga ttc ctg gca cct gtc ttc gct ctg ttc gta cca ttc tac tgc tcc 487  
Gly Phe Leu Ala Pro Val Phe Ala Leu Phe Val Pro Phe Tyr Cys Ser  
130 135 140  
ata cca aga gtc caa gtc gca caa att ctg ggt cgg ttg tcc atc aca 535  
Ile Pro Arg Val Gln Val Ala Gln Ile Leu Gly Pro Leu Ser Ile Thr  
145 150 155 160  
aac aag aca ttg att tat ata ttg gga ctg cag ctt ttc acc tct ggt 583  
Asn Lys Thr Leu Ile Tyr Ile Leu Gly Leu Gln Leu Phe Thr Ser Gly  
165 170 175  
tcc tac atc tgg att gta gcc ata agt gga ctt atg tcc ggt ctg tgc 631  
Ser Tyr Ile Trp Ile Val Ala Ile Ser Gly Leu Met Ser Gly Leu Cys

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5 tac gac agc aaa atg ttc cag atg cat cag gtc etc tgc atc ccc age 679  
 Tyr Asp Ser Lys Met Phe Gln Val His Gln Val Leu Cys Ile Pro Ser 205  
 195  
 5 tgg atg gca aaa ttc ttt tct tgg aca ctt gaa ccc atc ttc tct tct 727  
 Trp Met Ala Lys Phe Phe Ser Trp Thr Leu Glu Pro Ile Phe Ser Ser 220  
 210  
 10 tea gaa ccc acc agc gaa gcc aga att ggg atg gga gcc acg ctg gac 775  
 Ser Glu Pro Thr Ser Glu Ala Arg Ile Gly Met Gly Ala Thr Leu Asp 235  
 225 atc cag aga cag cag aga atg gag ctg gac cgg cag ctg atg ttc 240  
 Ile Gln Arg Gln Gln Arg Met Glu Leu Leu Asp Arg Gln Leu Met Phe 255  
 245  
 15 tct cag ttt gca caa ggg agg cga cag aga cag cag gga gga atg 871  
 Ser Gln Phe Ala Gln Gln Arg Arg Gln Arg Gln Gln Gln Gly Met 270  
 260  
 20 etc aat tgg aat cgt ctt ttt cct cct tta cgt cag cga caa aac gta 919  
 Ile Asn Trp Asn Arg Leu Phe Pro Pro Leu Arg Gln Arg Gln Asn Val 285  
 275  
 20 aac tat cag ggc ggt cgg cag tct gag cca gca gcg ccc cct cta gaa 967  
 Asn Tyr Gln Gly Arg Gln Ser Glu Pro Ala Ala Pro Pro Leu Glu 300  
 290  
 25 gtt tct gag gaa cag gtc gcc cgg etc atg gag atg gga ttt tcc aga 1015  
 Val Ser Glu Glu Gln Val Ala Arg Leu Met Glu Met Gly Phe Ser Arg 315  
 305 ggt gat gct ttg gaa gcc ctg aga gct tca aac aat gac etc aat gtc 1063  
 Gly Asp Ala Leu Glu Ala Leu Arg Ala Ser Asn Asn Asp Leu Asn Val 335  
 325  
 30 gcc acc aac ttc ctg ctg cag cac tgatgtccc aggcacacac tgg 1110  
 Ala Thr Asn Phe Leu Leu Gln His 340  
 35 gaccggaccg gcagccaggt gacagtgcgt ggtcccacc atcagatcag cccgggacc 1170  
 gagcatctct ggtgtgatg ttttgtggg angagggggg ttccaccgca cccctgacct 1230  
 caaccgcaag actgtgccc ttttagtgg gagataagtt tgcattaca ttgcatgta 1290  
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gaatgttt aaatgcatt aaatggag attctgcag gaagtgaat ggcactccag 1410  
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 cctggcgc accatgtaaa gacacggctc ctgcacagc ctaggagggc gcgtgacag 180  
 ggcgtaggg aactgggag cgcgcgcgc atg ggg ccg cct ggg gcc 231  
 Met Gly Pro Pro Gly Ala  
 30 1 5  
 ggg gtc tcc tgc cgc ggt ggc tgc ggc ttt tcc aga ttg ctg gca tgg 279  
 Gly Val Ser Cys Arg Gly Cys Gly Phe Ser Arg Leu Leu Ala Trp 20  
 10  
 tgc ttc ctg ctg gcc atg cag cag gca ccc ggt tcc cgg ggg gct 327  
 Cys Phe Leu Leu Ala Leu Ser Pro Gln Ala Pro Gly Ser Arg Gly Ala



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25 30 35  
gaa gga gtc tgg acc ggc tcc aac gtc tcc tgg cgg gtc ccc ccc 375  
gln ala val trp thr ala tyr leu asn val ser trp arg val pro his  
40 45 50 55  
acc gga gtc aac cgt acc gtc tgg ggc ctc arg gaa ggc gtc tcc 423  
thr gly val asn arg thr val trp gln leu ser gln gln gly val tyr  
60 65 70  
ggc cag gac tgg cgg ctc ggc cct gtc gct ggg gtc ctc gta ccc 471  
gly gln asp ser pro leu gln pro val ala gly val leu val pro pro  
75 80 85  
gac ggg ccc ggg ggc ctc aac ggc tgt aac cgg ccc acc aat ttc acc 519  
asp gly pro gly ala leu asn ala cys asn pro his thr asn phe thr  
90 95 100  
gtc ccc acc gtc tgg gga agc acc gtc caa gtc tct tgg ttc ggc ctc 567  
val pro thr val trp gly ser thr val gln val ser trp leu ala leu  
105 110 115  
acc caa cgc ggc ggg ggc tgc acc ttc gca gac aag atc cat ctc gct 615  
ile gln arg gly gly cys thr phe ala asp lys ile his leu ala  
120 125 130 135  
cat gaa aga ggg ggc tct gga ggc gtc atc ttt aac ttc ccc ggg acc 663  
tyr gln arg gly ala ser gly ala val ile phe asn phe pro gly thr  
140 145 150  
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arg asn gln val ile pro met ser his pro gly ala val asp ile val  
155 160 165  
gca atc atg atc ggc aat ctc aaa ggc aca aaa att ctc caa tct att 759  
ala ile met ile gly asn leu lys gly thr lys ile leu gln ser ile  
170 175 180  
caa aga ggc ata caa gtc aca atg gtc ata gaa gta ggg aaa aac cat 807  
gln arg gly ile gln val thr met val ile gln val gly lys lys his  
185 190 195  
ggc cct tgg gtc aat ccc tat tca att ttt ttc gtc tct gtc tcc ttt 855  
gly pro trp val asn his tyr ser ile phe phe val ser val ser phe  
200 205 210 215  
ttt att atc acc ggg gca act gtc ggc tat ttt atc ttt tat tct gct 903

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phe ile ile thr ala ala thr val gly tyr phe ile phe tyr ser ala  
220 225 230  
cga agc cta cgg aat gca aga gct caa agc aag aag cag agc caa tta 951  
arg arg leu arg asn ala arg ala gln ser arg lys gln arg gln leu  
235 240 245  
aag gca gac gct aaa aac gct att gga aag ctc caa cta cgc aca ctc 999  
lys ala asp ala lys lys ala ile gly arg leu leu arg thr leu  
250 255 260  
aaa caa gga gac aag gaa att ggc cct gac gga gat agt tgt gct gtc 1047  
lys gln gly asp lys gln ile gly pro asp gly asp ser cys ala val  
265 270 275  
tgc att gaa ttc tat aac cca aat gat ttc gta cgc atc tta acc tgc 1095  
cys ile gln leu tyr lys pro asn asp leu val arg ile leu thr cys  
280 285 290 295  
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asn his ile phe his lys thr cys val asp pro trp leu leu gln his  
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arg thr cys pro met cys lys cys asp ile leu lys ala leu gly ile  
315 320 325  
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330 335 340  
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asn gln ile ser asn ser ala ser ser his gln gln asp asn arg ser  
345 350 355  
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cct ctc gag gaa ccc gtc cag tca aca aat gaa agt cta cag ctc gta 1383  
pro leu gln gln his val gln ser thr asn gln ser leu gln leu val  
380 385 390  
aac cat gaa gaa aat tct gtc gca gtc gat gtt att cct cat gtc gac 1431  
asn his gln ala asn ser val ala val asp val ile pro his val asp  
395 400 405

asc cca acc ttt gaa gaa gaa gaa act cct aat caa gag act gct gtt 1479  
 Aan Pro Thr Phe Glu Asp Glu Thr Pro Asn Gln Glu Thr Ala Val  
 410 415 420  
 cga gaa att aaa tct taaaatctgt gtaaatagaa aacttgaacc attagt 1530  
 Arg Glu Ile Lys Ser  
 425  
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